

=> d his ful

(FILE 'HOME' ENTERED AT 16:26:45 ON 08 DEC 2005)

FILE 'HCAPLUS' ENTERED AT 16:26:50 ON 08 DEC 2005

L1 1 SEA ABB=ON PLU=ON US200!-798470/APPS  
SEL RN

FILE 'REGISTRY' ENTERED AT 16:27:08 ON 08 DEC 2005

L2 29 SEA ABB=ON PLU=ON (103775-10-6/BI OR 111223-26-8/BI OR  
111902-57-9/BI OR 127420-24-0/BI OR 140369-78-4/BI OR 142695-08  
-7/BI OR 182176-67-6/BI OR 182176-70-1/BI OR 182176-83-6/BI OR  
39698-78-7/BI OR 62571-86-2/BI OR 74258-86-9/BI OR 75847-73-3/B  
I OR 76420-72-9/BI OR 76547-98-3/BI OR 82768-85-2/BI OR  
82834-16-0/BI OR 83435-66-9/BI OR 83647-97-6/BI OR 85441-61-8/B  
I OR 86541-75-5/BI OR 87333-19-5/BI OR 87679-37-6/BI OR  
88768-40-5/BI OR 89371-37-9/BI OR 9015-82-1/BI OR 95153-31-4/BI  
OR 95399-71-6/BI OR 98048-97-6/BI)

FILE 'HCAPLUS' ENTERED AT 16:27:13 ON 08 DEC 2005

L3 1 SEA ABB=ON PLU=ON L1 AND L2  
D IALL HITSTR  
E INFLAMMATORY BOWEL DISEASE/CT  
E E3+ALL  
E E2+ALL

L4 7752 SEA ABB=ON PLU=ON "INTESTINE, DISEASE (L) INFLAMMATORY"+PFT/C  
T  
E SHORT BOWEL SYNDROME/CT  
E E4+ALL  
E E2+ALL

L5 261 SEA ABB=ON PLU=ON "INTESTINE, DISEASE (L) SHORT BOWEL  
SYNDROME"+PFT/CT  
E CROHNS DISEASE/CT  
E E1+ALL  
E E2+ALL

L6 4 SEA ABB=ON PLU=ON "INFLAMMATION (L) CROHN'S DISEASE"+PFT/CT  
E CROHNS DISEASE/CT  
E E1+ALL  
E E3+ALL

L7 4 SEA ABB=ON PLU=ON "INTESTINE, DISEASE (L) CROHN'S"+PFT/CT  
E CELIAC DISEASE/CT  
E E3+ALL

L8 2349 SEA ABB=ON PLU=ON CELIAC DISEASE+PFT/CT  
E ULCERATIVE COLITIS/CT  
E E3+ALL  
E E2+ALL

L9 4545 SEA ABB=ON PLU=ON "INFLAMMATION (L) ULCERATIVE COLITIS"+PFT/C  
T  
E ULCERATIVE COLITIS/CT  
E E3+ALL  
E E3+ALL

L10 4544 SEA ABB=ON PLU=ON "INTESTINE, DISEASE (L) ULCERATIVE  
COLITIS"+PFT/CT  
E STOMACH ULCERS/CT  
E ULCER/CT  
E STOMACH, DISEA/CT  
E E25+ALL

L11 2302 SEA ABB=ON PLU=ON "STOMACH, DISEASE (L) ULCER"+PFT/CT  
E DIVERTICULITIS/CT

E E3+ALL  
 E E2+ALL  
 L12 130 SEA ABB=ON PLU=ON "INFLAMMATION (L) DIVERTICULITIS"+PFT/CT  
 E DIVERTICULITIS/CT  
 E E3+ALL  
 E E3+ALL  
 L13 130 SEA ABB=ON PLU=ON "INTESTINE, DISEASE (L) DIVERTICULITIS"+PFT  
 /CT  
 E POUCHITIS/CT  
 E PROCTITIS/CT  
 E E3+ALL  
 E E2+ALL  
 L14 199 SEA ABB=ON PLU=ON "INFLAMMATION (L) RECTAL"+PFT/CT  
 E PROCTITIS/CT  
 E E3+ALL  
 E E3+ALL  
 L15 177 SEA ABB=ON PLU=ON "INTESTINE, DISEASE (L) RECTUM, INFLAMMATIO  
 N"+PFT/CT  
 E CHRONIC DIARRHEA/CT  
 E DIARRHEA/CT  
 E E3+ALL  
 L16 78 SEA ABB=ON PLU=ON DIARRHEA+PFT/CT(L)CHRONIC  
 L17 21694 SEA ABB=ON PLU=ON (L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10  
 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16) OR INFLAMMATORY  
 BOWEL OR SHORT BOWEL OR "CROHN'S DISEASE" OR CROHNS DISEASE OR  
 CELIAC DISEAS? OR ULCER?(3A)COLITIS OR STOMACH(3A)ULCER? OR  
 DIVERTICULITIS OR POUCHITIS OR PROCTITIS OR CHRONIC(3A)DIARRHEA

E ANGIOTENSIN CONVERTING ENZYME

FILE 'REGISTRY' ENTERED AT 16:39:36 ON 08 DEC 2005

E ALACEPRIL/CN  
 L18 1 SEA ABB=ON PLU=ON ALACEPRIL/CN  
 L19 1 SEA ABB=ON PLU=ON BENAZEPRIL/CN  
 L20 1 SEA ABB=ON PLU=ON LOTENSIN/CN  
 L21 1 SEA ABB=ON PLU=ON CAPTOPRIL/CN  
 L22 1 SEA ABB=ON PLU=ON CILAZAPRIL/CN  
 L23 1 SEA ABB=ON PLU=ON CERANAPRIL  
 L24 1 SEA ABB=ON PLU=ON DELAPRIL/CN  
 L25 1 SEA ABB=ON PLU=ON ENALAPRIL/CN  
 L26 1 SEA ABB=ON PLU=ON ENALAPRILAT/CN  
 L27 1 SEA ABB=ON PLU=ON FOSINOPRIL/CN  
 L28 1 SEA ABB=ON PLU=ON FOSINOPRILAT/CN  
 L29 1 SEA ABB=ON PLU=ON IMIDAPRIL/CN  
 L30 1 SEA ABB=ON PLU=ON LISINOPRIL/CN  
 L31 1 SEA ABB=ON PLU=ON MOEXIPRIL/CN  
 L32 1 SEA ABB=ON PLU=ON PERINDOPRIL/CN  
 L33 1 SEA ABB=ON PLU=ON PERINDOPRILAT/CN  
 L34 1 SEA ABB=ON PLU=ON QUINAPRIL/CN  
 L35 1 SEA ABB=ON PLU=ON QUINAPRILAT/CN  
 L36 1 SEA ABB=ON PLU=ON RAMIPRIL/CN  
 L37 1 SEA ABB=ON PLU=ON SARALASIN ACETATE/CN  
 L38 1 SEA ABB=ON PLU=ON SPIRAPRIL/CN  
 L39 1 SEA ABB=ON PLU=ON TEMOCAPRIL/CN  
 L40 1 SEA ABB=ON PLU=ON TRANDOLAPRIL/CN  
 E BIOPROJECT BP1.137/CN  
 E CHIESI/CN  
 E BP1.137/RN  
 E BP1.137/CN

E BP1137/CN  
E BP1 137/CN  
E CHF 1514/CN  
L41 1 SEA ABB=ON PLU=ON CHF 1514  
E FPL-66564/CN  
E FPL 66564/CN  
L42 1 SEA ABB=ON PLU=ON FPL 66564/CN  
L43 1 SEA ABB=ON PLU=ON IDRAPRIL/CN  
E MDL-100240/CN  
E MDL 100240/CN  
L44 1 SEA ABB=ON PLU=ON MDL 100240/CN  
E S-5590/CN  
E S 5590/CN  
L45 1 SEA ABB=ON PLU=ON S 5590/CN  
L46 28 SEA ABB=ON PLU=ON (L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR  
L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR  
L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR L40 OR L41 OR  
L42 OR L43 OR L44 OR L45)  
  
FILE 'HCAPLUS' ENTERED AT 16:45:27 ON 08 DEC 2005  
L47 72 SEA ABB=ON PLU=ON L17 AND (L46 OR ANGIOTENSIN(S)?CONVERT?(S) (  
INHIB? OR BLOCK? OR ANTAG?) OR LOTENSIN OR CAPOTEN OR VASOTEC  
OR MONOPRIL OR PRINIVIL OR ZESTRIL OR UNIVASC OR ACCUPRIL OR  
ACEON OR ALTACE OR MAVIK OR ACE INHIB?)  
L48 1 SEA ABB=ON PLU=ON L47 AND L1  
D KWIC L47 10  
L49 64 SEA ABB=ON PLU=ON L47 AND THU/RL  
L50 8 SEA ABB=ON PLU=ON L47 NOT L49

FILE 'MEDLINE' ENTERED AT 16:51:22 ON 08 DEC 2005

FILE 'REGISTRY' ENTERED AT 16:51:37 ON 08 DEC 2005  
SET SMARTSELECT ON  
L51 SEL PLU=ON L46 1- CHEM : 183 TERMS  
SET SMARTSELECT OFF

FILE 'MEDLINE' ENTERED AT 16:51:40 ON 08 DEC 2005

L52 21896 SEA ABB=ON PLU=ON L51  
L53 21896 SEA ABB=ON PLU=ON L46 OR L52  
D SCA  
D TRIAL  
E ANGIOTENSI CONVERT/CT  
E ANGIOTENSIN CONVERT/CT  
E E6+ALL  
E E2+ALL  
L54 29253 SEA ABB=ON PLU=ON "ANGIOTENSIN-CONVERTING ENZYME INHIBITORS"+  
PFT,NT/CT  
L55 32469 SEA ABB=ON PLU=ON L54 OR L53  
L56 72785 SEA ABB=ON PLU=ON INFLAMMATORY BOWEL OR SHORT BOWEL OR  
"CROHN'S DISEASE" OR CROHNS DISEASE OR CELIAC DISEAS? OR  
ULCER?(3A)COLITIS OR STOMACH(3A)ULCER? OR DIVERTICULITIS OR  
POUCHITIS OR PROCTITIS OR CHRONIC(3A)DIARRHEA  
L57 18 SEA ABB=ON PLU=ON L55 AND L56

FILE 'EMBASE' ENTERED AT 16:54:39 ON 08 DEC 2005

FILE 'REGISTRY' ENTERED AT 16:54:45 ON 08 DEC 2005  
SET SMARTSELECT ON  
L58 SEL PLU=ON L46 1- CHEM : 183 TERMS

SET SMARTSELECT OFF

FILE 'EMBASE' ENTERED AT 16:54:46 ON 08 DEC 2005

L59 43028 SEA ABB=ON PLU=ON L58  
L60 43028 SEA ABB=ON PLU=ON L46 OR L59  
E ANGIOTENSIN CONVERT/CT  
E E23+ALL  
E E2+ALL  
L61 65974 SEA ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR+PFT,N  
T,NXT/CT  
L62 66865 SEA ABB=ON PLU=ON L60 OR L61  
L63 57400 SEA ABB=ON PLU=ON INFLAMMATORY BOWEL OR SHORT BOWEL OR  
"CROHN'S DISEASE" OR CROHNS DISEASE OR CELIAC DISEAS? OR  
ULCER?(3A) COLITIS OR STOMACH(3A) ULCER? OR DIVERTICULITIS OR  
POUCHITIS OR PROCTITIS OR CHRONIC(3A) DIARRHEA  
L64 138 SEA ABB=ON PLU=ON L62 AND L63  
D KWIC  
L65 23 SEA ABB=ON PLU=ON L64 AND ANGIOTENSIN?

FILE HOME

FILE HCAPLUS

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FILE COVERS 1907 - 8 Dec 2005 VOL 143 ISS 24

FILE LAST UPDATED: 7 Dec 2005 (20051207/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 7 DEC 2005 HIGHEST RN 869534-51-0

DICTIONARY FILE UPDATES: 7 DEC 2005 HIGHEST RN 869534-51-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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\* The CA roles and document type information have been removed from \*

\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\* \*  
\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

#### FILE MEDLINE

FILE LAST UPDATED: 6 DEC 2005 (20051206/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

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#### FILE EMBASE

FILE COVERS 1974 TO 1 Dec 2005 (20051201/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

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=> fil hcap

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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FILE COVERS 1907 - 8 Dec 2005 VOL 143 ISS 24  
 FILE LAST UPDATED: 7 Dec 2005 (20051207/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate  
 substance identification.

=> d que stat 147

L4	7752	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INTESTINE, DISEASE (L) INFLAMMATORY"+PFT/CT
L5	261	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INTESTINE, DISEASE (L) SHORT BOWEL SYNDROME"+PFT/CT
L6	4	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INFLAMMATION (L) CROHN'S DISEASE"+PFT/CT
L7	4	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INTESTINE, DISEASE (L) CROHN'S"+PFT/CT
L8	2349	SEA FILE=HCAPLUS ABB=ON	PLU=ON	CELIAC DISEASE+PFT/CT
L9	4545	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INFLAMMATION (L) ULCERATIVE COLITIS"+PFT/CT
L10	4544	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INTESTINE, DISEASE (L) ULCERATIVE COLITIS"+PFT/CT
L11	2302	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"STOMACH, DISEASE (L) ULCER"+PFT/CT
L12	130	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INFLAMMATION (L) DIVERTICULIT IS"+PFT/CT
L13	130	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INTESTINE, DISEASE (L) DIVERTICULITIS"+PFT/CT
L14	199	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INFLAMMATION (L) RECTAL"+PFT/ CT
L15	177	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"INTESTINE, DISEASE (L) RECTUM, INFLAMMATION"+PFT/CT
L16	78	SEA FILE=HCAPLUS ABB=ON	PLU=ON	DIARRHEA+PFT/CT (L) CHRONIC
L17	21694	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16) OR INFLAMMATORY BOWEL OR SHORT BOWEL OR "CROHN'S DISEASE" OR CROHNS DISEASE OR CELIAC DISEAS? OR ULCER? (3A) COLITIS OR STOMACH (3A) ULCER? OR DIVERTICULITIS OR POUCHITIS OR PROCTITIS OR CHRONIC (3A) DIARRHEA
L18	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	ALACEPRIL/CN
L19	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	BENAZEPRIL/CN
L20	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	LOTENSIN/CN
L21	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	CAPTOPRIL/CN
L22	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	CILAZAPRIL/CN
L23	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	CERANAPRIL
L24	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	DELAPRIL/CN
L25	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	ENALAPRIL/CN
L26	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	ENALAPRILAT/CN
L27	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRIL/CN
L28	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRILAT/CN
L29	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	IMIDAPRIL/CN
L30	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	LISINOPRIL/CN
L31	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	MOEXIPRIL/CN
L32	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRIL/CN
L33	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRILAT/CN
L34	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	QUINAPRIL/CN
L35	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	QUINAPRILAT/CN
L36	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	RAMIPRIL/CN

L37 1 SEA FILE=REGISTRY ABB=ON PLU=ON SARALASIN ACETATE/CN  
L38 1 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL/CN  
L39 1 SEA FILE=REGISTRY ABB=ON PLU=ON TEMOCAPRIL/CN  
L40 1 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL/CN  
L41 1 SEA FILE=REGISTRY ABB=ON PLU=ON CHF 1514  
L42 1 SEA FILE=REGISTRY ABB=ON PLU=ON FPL 66564/CN  
L43 1 SEA FILE=REGISTRY ABB=ON PLU=ON IDRAPRIL/CN  
L44 1 SEA FILE=REGISTRY ABB=ON PLU=ON MDL 100240/CN  
L45 1 SEA FILE=REGISTRY ABB=ON PLU=ON S 5590/CN  
L46 28 SEA FILE=REGISTRY ABB=ON PLU=ON (L18 OR L19 OR L20 OR L21 OR  
L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR  
L31 OR L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR  
L40 OR L41 OR L42 OR L43 OR L44 OR L45)  
L47 72 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND (L46 OR ANGIOTENSIN(S)  
?CONVERT?(S) (INHIB? OR BLOCK? OR ANTAG?) OR LOTENSIN OR  
CAPOTEN OR VASOTEC OR MONOPRIL OR PRINIVIL OR ZESTRIL OR  
UNIVASC OR ACCUPRIL OR ACEON OR ALTACE OR MAVIK OR ACE INHIB?)

=> fil medline

FILE 'MEDLINE' ENTERED AT 17:02:40 ON 08 DEC 2005

FILE LAST UPDATED: 6 DEC 2005 (20051206/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP  
RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the  
MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> d que stat l57

L18 1 SEA FILE=REGISTRY ABB=ON PLU=ON ALACEPRIL/CN  
L19 1 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL/CN  
L20 1 SEA FILE=REGISTRY ABB=ON PLU=ON LOTENSIN/CN  
L21 1 SEA FILE=REGISTRY ABB=ON PLU=ON CAPTOPRIL/CN  
L22 1 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL/CN  
L23 1 SEA FILE=REGISTRY ABB=ON PLU=ON CERANAPRIL  
L24 1 SEA FILE=REGISTRY ABB=ON PLU=ON DELAPRIL/CN  
L25 1 SEA FILE=REGISTRY ABB=ON PLU=ON ENALAPRIL/CN  
L26 1 SEA FILE=REGISTRY ABB=ON PLU=ON ENALAPRILAT/CN  
L27 1 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL/CN  
L28 1 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRILAT/CN  
L29 1 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL/CN  
L30 1 SEA FILE=REGISTRY ABB=ON PLU=ON LISINOPRIL/CN  
L31 1 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL/CN  
L32 1 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL/CN  
L33 1 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRILAT/CN  
L34 1 SEA FILE=REGISTRY ABB=ON PLU=ON QUINAPRIL/CN  
L35 1 SEA FILE=REGISTRY ABB=ON PLU=ON QUINAPRILAT/CN

```
L36      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  RAMIPRIL/CN
L37      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SARALASIN ACETATE/CN
L38      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SPIRAPRIL/CN
L39      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TEMOCAPRIL/CN
L40      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRANDOLAPRIL/CN
L41      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CHF 1514
L42      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  FPL 66564/CN
L43      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  IDRAPRIL/CN
L44      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MDL 100240/CN
L45      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  S 5590/CN
L46      28 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L18 OR L19 OR L20 OR L21 OR
      L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR
      L31 OR L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR
      L40 OR L41 OR L42 OR L43 OR L44 OR L45)
L51      SEL  PLU=ON  L46 1- CHEM :      183 TERMS
L52      21896 SEA FILE=MEDLINE ABB=ON  PLU=ON  L51
L53      21896 SEA FILE=MEDLINE ABB=ON  PLU=ON  L46 OR L52
L54      29253 SEA FILE=MEDLINE ABB=ON  PLU=ON  "ANGIOTENSIN-CONVERTING
      ENZYME INHIBITORS"+PFT,NT/CT
L55      32469 SEA FILE=MEDLINE ABB=ON  PLU=ON  L54 OR L53
L56      72785 SEA FILE=MEDLINE ABB=ON  PLU=ON  INFLAMMATORY BOWEL OR SHORT
      BOWEL OR "CROHN'S DISEASE" OR CROHNS DISEASE OR CELIAC DISEAS?
      OR ULCER?(3A) COLITIS OR STOMACH(3A) ULCER? OR DIVERTICULITIS OR
      POUCHITIS OR PROCTITIS OR CHRONIC(3A) DIARRHEA
L57      18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L55 AND L56
```

=> fil embase

FILE 'EMBASE' ENTERED AT 17:02:48 ON 08 DEC 2005

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FILE COVERS 1974 TO 1 Dec 2005 (20051201/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

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substance identification.

=> d que stat l65

```
L18      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALACEPRIL/CN
L19      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  BENAZEPRIL/CN
L20      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  LOTENSIN/CN
L21      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CAPTOPRIL/CN
L22      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CILAZAPRIL/CN
L23      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CERANAPRIL
L24      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DELAPRIL/CN
L25      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ENALAPRIL/CN
L26      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ENALAPRILAT/CN
L27      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  FOSINOPRIL/CN
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L29      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  IMIDAPRIL/CN
L30      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  LISINOPRIL/CN
L31      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MOEXIPRIL/CN
L32      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  PERINDOPRIL/CN
L33      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  PERINDOPRILAT/CN
L34      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  QUINAPRIL/CN
L35      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  QUINAPRILAT/CN
L36      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  RAMIPRIL/CN
L37      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SARALASIN ACETATE/CN
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L39 1 SEA FILE=REGISTRY ABB=ON PLU=ON TEMOCAPRIL/CN  
L40 1 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL/CN  
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L46 28 SEA FILE=REGISTRY ABB=ON PLU=ON (L18 OR L19 OR L20 OR L21 OR  
L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR  
L31 OR L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR  
L40 OR L41 OR L42 OR L43 OR L44 OR L45)  
L58 SEL PLU=ON L46 1- CHEM : 183 TERMS  
L59 43028 SEA FILE=EMBASE ABB=ON PLU=ON L58  
L60 43028 SEA FILE=EMBASE ABB=ON PLU=ON L46 OR L59  
L61 65974 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
INHIBITOR+PFT,NT,NXT/CT  
L62 66865 SEA FILE=EMBASE ABB=ON PLU=ON L60 OR L61  
L63 57400 SEA FILE=EMBASE ABB=ON PLU=ON INFLAMMATORY BOWEL OR SHORT  
BOWEL OR "CROHN'S DISEASE" OR CROHNS DISEASE OR CELIAC DISEAS?  
OR ULCER? (3A) COLITIS OR STOMACH (3A) ULCER? OR DIVERTICULITIS OR  
POUCHITIS OR PROCTITIS OR CHRONIC (3A) DIARRHEA  
L64 138 SEA FILE=EMBASE ABB=ON PLU=ON L62 AND L63  
L65 23 SEA FILE=EMBASE ABB=ON PLU=ON L64 AND ANGIOTENSIN?

=> dup rem l47 l57 l65

FILE 'HCAPLUS' ENTERED AT 17:02:59 ON 08 DEC 2005

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FILE 'MEDLINE' ENTERED AT 17:02:59 ON 08 DEC 2005

FILE 'EMBASE' ENTERED AT 17:02:59 ON 08 DEC 2005

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PROCESSING COMPLETED FOR L47

PROCESSING COMPLETED FOR L57

PROCESSING COMPLETED FOR L65

L66 103 DUP REM L47 L57 L65 (10 DUPLICATES REMOVED)

ANSWERS '1-72' FROM FILE HCAPLUS

ANSWERS '73-86' FROM FILE MEDLINE

ANSWERS '87-103' FROM FILE EMBASE

=> s l66 and py<2005

L67 72 L66 AND PY<2005

=> d l67 ibib abs hitind 1-72

L67 ANSWER 1 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:1223666 HCAPLUS

TITLE: Drug discovery assays based on the biology of chronic  
disease

INVENTOR(S): Polansky, Hanan

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 307 pp., Cont.-in-part of U.S.  
Ser. No. 223,050.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005255458	A1	20051117	US 2003-611217	20030701
US 2003068616	A1	20030410	US 2002-223050	20020814 <--
PRIORITY APPLN. INFO.:			US 2002-223050	A2 20020814
			US 2000-732360	A2 20001207

AB Using the recently discovered biol. of chronic disease, the invention presents new methods for evaluating the effectiveness of a compound for use in modulating the progression of chronic disease, for determining whether a subject has a chronic disease, or has an increased risk of developing clin. symptoms associated with such disease, and for treating chronic disease.

IC ICM C12Q001-70  
ICS C12Q001-68

INCL 435005000; 435006000

CC 1-1 (Pharmacology)  
Section cross-reference(s): 14

IT INDEXING IN PROGRESS

IT Intestine, disease

(inflammatory; drug discovery assays based on biol. of chronic disease)

IT 50-28-2, Estradiol-17 $\beta$ -3,17-diol (17 $\beta$ )- 50-78-2, Aspirin  
51-41-2, Norepinephrine 58-22-0, Testosterone 66-81-9, Cycloheximide  
156-54-7, Sodium butyrate 302-79-4, all-trans-Retinoic acid 362-74-3,  
Dibutyl cyclic amp 521-18-6, Dihydrotestosterone 965-93-5, R1881  
7481-89-2, DdC 7683-59-2, Isoprenaline 9002-68-0, FSH 11128-99-7,  
Angiotensin II 13721-39-6, Sodium orthovanadate 16561-29-8, TPA  
(phorbol derivative) 30516-87-1, Azt 56092-81-0, Ionomycin  
56180-94-0, Acarbose 62571-86-2, Captopril 66575-29-9,  
Forskolin 69655-05-6, DdI 79902-63-9, Simvastatin 81093-37-0,  
Pravastatin 81872-10-8, Zofenopril 87333-19-5, Ramipril  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(drug discovery assays based on biol. of chronic disease)

L67 ANSWER 2 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:122803 HCAPLUS

DOCUMENT NUMBER: 142:219083

TITLE: Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive and anticancer agents

INVENTOR(S): Metcalf, Chester A.; Rozamus, Leonard W.; Wang, Yihan; Bernstein, David L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 635,054.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005032825	A1	20050210	US 2004-862149	20040604
US 2003220297	A1	20031127	US 2003-357152	20030203 <--

US 2004073024  
PRIORITY APPLN. INFO.:

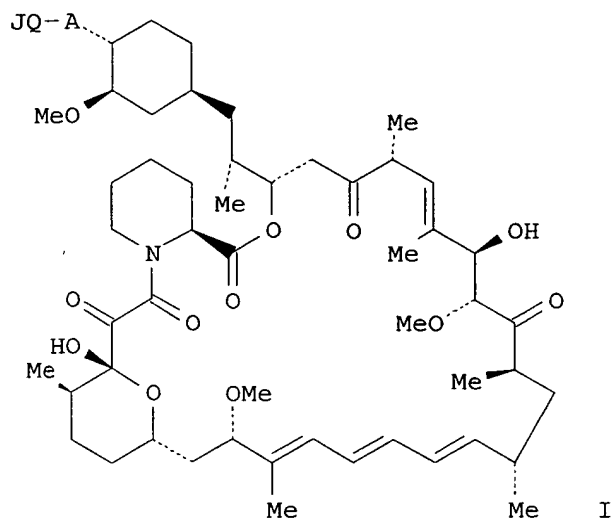
A1 20040415

US 2003-635054  
US 2002-353252P  
US 2002-426928P  
US 2002-428383P  
US 2002-438930P  
US 2003-357152  
US 2003-635054

20030806 <--  
P 20020201  
P 20021115  
P 20021122  
P 20021217  
A2 20030203  
A2 20030806

OTHER SOURCE(S):  
GI

MARPAT 142:219083



AB Rapamycin derivs. containing phosphorus moiety, such as I [A = O, S, NR<sub>2</sub>, absent; Q = V, OV, SV, NR<sub>2</sub>, absent; V = aliphatic, heteroaliph., aryl, heteroaryl moiety, such that J is linked to the cyclohexyl ring directly, through A or through VA, OVA, SVA or NR<sub>2</sub>VA; J = P(:K)(YR<sub>5</sub>)<sub>2</sub>, P(YR<sub>5</sub>)<sub>2</sub>, P(:K)(YR<sub>5</sub>)GR<sub>6</sub>; K = O, S; Y = O, S, NR<sub>2</sub>, bond; R<sub>2</sub>, R<sub>5</sub> = aliphatic, heteroaliph., aryl, heteroaryl, H; R<sub>6</sub> = PK(YR<sub>5</sub>)YR<sub>5</sub>, SO<sub>2</sub>YR<sub>5</sub>, C(O)YR<sub>5</sub>; G = O, S, NR<sub>2</sub>, (M)X; M = (un)substituted methylene, alkyl, alkylene; X = 1-6], and pharmaceutically acceptable derivs. thereof, were prepared for therapeutic use as immunosuppressive and anticancer agents. These rapamycin derivs. are useful for treatment of graft vs. host disease, lupus, rheumatoid arthritis, diabetes mellitus, myasthenia gravis, multiple sclerosis, psoriasis, dermatitis, eczema, seborrhea, **inflammatory bowel** disease, pulmonary inflammation, ocular uveitis; adult T-cell leukemia, lymphoma, fungal infections, hyperproliferative restenosis, graft vascular atherosclerosis, coronary artery disease, cerebrovascular disease, arteriosclerosis, atherosclerosis, nonatheromatous arteriosclerosis, or vascular wall damage from cellular events leading toward immune mediated vascular damage, stroke or multi-infarct dementia. Thus, I [A-QJ = OP(O)(OBu)Me] was prepared by reacting rapamycin with methylphosphonic dichloride and n-butanol using 3,5-lutidine in CH<sub>2</sub>Cl<sub>2</sub> under a nitrogen atmosphere. Binding affinity of the rapamycin phosphorus derivs. for human FKBP-12 protein was assayed, dosages for restenosis prevention were discussed.

IC ICM A61K031-675  
ICS A61K031-4745

INCL 514291000; 540456000; 514080000

CC 26-6 (Biomolecules and Their Synthetic Analogs)

Section cross-reference(s): 1, 63

IT **Intestine, disease**

(**inflammatory**; preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive and anticancer agents)

IT 50-07-7, Mitomycin C 50-28-2, Estradiol, biological studies 51-21-8, 5-Fluorouracil 51-43-4D, Epinephrine, cisplatin gel 52-53-9, Verapamil 55-98-1, Busulfan 57-63-6, Ethinyl estradiol 58-05-9, Leucovorin 59-05-2, Methotrexate 81-81-2, Warfarin 127-07-1, Hydroxyurea 147-94-4D, Cytarabine, liposomal 148-82-3, Melphalan 154-93-8D, Gliadel, Wafer 298-81-7, Methoxsalen 302-79-4, Tretinoin 305-03-3, Chlorambucil 315-30-0, Zylloprim 525-66-6, Propranolol 637-07-0, Clofibrate 645-05-6, Altretamine 943-45-3D, Fibric acid, derivs. 1327-53-3, Arsenic trioxide 2998-57-4, Estramustine 3778-73-2, Ifosfamide 3930-20-9, Sotalol 4291-63-8, Cladribine 7280-37-7, Estropipate 9005-49-6, Heparin, biological studies 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 14769-73-4, Levamisole 14807-96-6, Talc, biological studies 15663-27-1, Cisplatin 19767-45-4, Mesna 20537-88-6, Amifostine 20830-81-3, Daunorubicin 20830-81-3D, Daunorubicin, liposomal 21679-14-1, Fludarabine 21829-25-4, Nifedipine 23214-92-8, Doxorubicin 24584-09-6, Dexrazoxane 25812-30-0, Gemfibrozil 26839-75-8, Timolol 29122-68-7, Atenolol 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 37517-30-9, Acebutolol 38363-40-5, Penbutolol 40391-99-9, Pamidronate 41575-94-4, Carboplatin 42200-33-9, Nadolol 42399-41-7, Diltiazem 51384-51-1, Metoprolol 51781-06-7, Carteolol 53910-25-1, Pentostatin 55985-32-5, Nicardipine 56124-62-0, Valrubicin 56420-45-2, Epirubicin 57852-57-0, Idamycin 58957-92-9, Idarubicin 62571-86-2, Captopril 63659-18-7, Betaxolol 63675-72-9, Nisoldipine 64706-54-3, Bepridil 65271-80-9, Mitoxantrone 66085-59-4, Nimodipine 66722-44-9, Bisoprolol 71486-22-1, Vinorelbine 72509-76-3, Felodipine 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81147-92-4, Esmolol 82834-16-0, Perindopril 85441-61-8, Quinapril 85622-93-1, Temozolomide 87333-19-5, Ramipril 87679-37-6, Trandolapril 87806-31-3, Porfimer sodium 88150-42-9, Amlodipine 89778-26-7, Toremfene 93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 98048-97-6, Fosinopril 103775-10-6, Moexipril 107868-30-4, Exemestane 112809-51-5, Letrozole 114798-26-4, Losartan 114977-28-5, Docetaxel 117091-64-2, Etoposide phosphate 118072-93-8, Zoledronate 123948-87-8, Topotecan 129453-61-8, Fulvestrant 134523-00-5, Atorvastatin 137862-53-4, Valsartan 138402-11-6, Irbesartan 139481-59-7, Candesartan 144701-48-4, Telmisartan 145599-86-6, Cerivastatin 145781-92-6, Goserelin acetate 153559-49-0, Bexarotene 154361-50-9, Capecitabine 169590-42-5, Celecoxib 174722-31-7, Rituximab 180288-69-1, Trastuzumab 216503-57-0, Alemtuzumab 216974-75-3, Avastin 220127-57-1, Imatinib mesylate 220578-59-6, Gemtuzumabozogamicin 346689-77-8, XR11576 387867-13-2, MLN518 391208-93-8, Glycogen synthase kinase 3 612092-74-7, MLN 591 679809-58-6, Enoxaparin 811442-46-3, MLN 2704

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive and anticancer agents)

L67 ANSWER 3 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:78296 HCAPLUS  
 DOCUMENT NUMBER: 142:170088  
 TITLE: Methods for the treatment of gastrointestinal disorders using guanylate cyclase C receptor activators, such as ST peptide variants  
 INVENTOR(S): Currie, Mark G.; Mahajan-Miklos, Shalina  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 83 pp., Cont.-in-part of U.S. Ser. No. 766,735.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005020811	A1	20050127	US 2004-796719	20040309
US 2004266989	A1	20041230	US 2004-766735	20040128 <--
WO 2005087797	A1	20050922	WO 2005-US7752	20050308

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:  
 US 2003-443098P P 20030128  
 US 2003-471288P P 20030515  
 US 2003-519460P P 20031112  
 US 2004-766735 A2 20040128  
 US 2004-796719 A 20040309  
 US 2004-845895 A 20040514  
 US 2004-899806 A 20040727  
 US 2005-54071 A 20050208

OTHER SOURCE(S): MARPAT 142:170088

AB The present invention features compns. and related methods for treating irritable bowel syndrome (IBS) and other gastrointestinal disorders and conditions using peptides and other agents that activate the guanylate cyclase C (GC-C) receptor. The gastrointestinal disorders include gastrointestinal motility disorders, functional gastrointestinal disorders, gastro-esophageal reflux disease (GERD), Crohn's disease, **ulcerative colitis, inflammatory bowel** disease, functional heartburn, dyspepsia (including functional dyspepsia or nonulcer dyspepsia), gastro-paresis, chronic intestinal pseudo-obstruction (or colonic pseudo-obstruction), and disorders and conditions associated with constipation, e.g., constipation associated with use of opiate pain killers, post-surgical constipation, and constipation associated with neuropathic disorders as well as other conditions and disorders. Provided are sequences of the peptides of the invention, as well as a method for their preparation. The peptides of the invention, like the bacterial ST peptides, have six Cys residues. These six Cys residues form three disulfide bonds in the mature and active form of the peptide. If the six Cys residues are identified, from the amino to carboxy terminus of the peptide, as A, B, C, D, E, and F, then the disulfide bonds form as

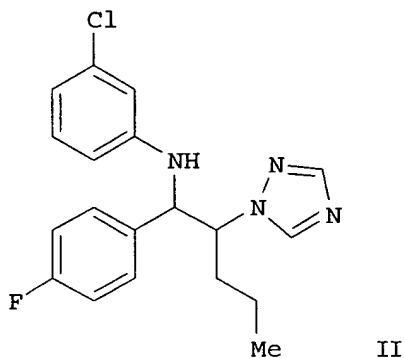
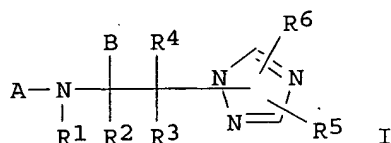
follows: A-D, B-E, and C-F. The formation of these bonds is thought to be important for GC-C receptor binding. Certain of the peptides of the invention include a potentially functional chymotrypsin cleavage site. Cleavage at chymotrypsin cleavage site reduces or eliminates the ability of the peptide to bind to the GC-C receptor. It is expected that chymotrypsin cleavage will moderate the action of a peptide of the invention having an appropriately positioned chymotrypsin cleavage site as the peptide passes through the intestinal tract.

IC ICM C07K007-08  
ICS C07K007-06  
INCL 530327000; 530328000  
CC 1-9 (Pharmacology)  
IT **Intestine, disease**  
(**inflammatory**; methods for treatment of gastrointestinal disorders using guanylate cyclase C (GC-C) receptor activators, such as ST peptide variants)  
IT **Inflammation**  
**Intestine, disease**  
(**ulcerative colitis**; methods for treatment of gastrointestinal disorders using guanylate cyclase C (GC-C) receptor activators, such as ST peptide variants)  
IT 9015-82-1, **Angiotensin-converting enzyme** 9068-52-4,  
CGMP Phosphodiesterase 37255-34-8, 5 $\alpha$ -Reductase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**inhibitors**; methods for treatment of gastrointestinal disorders using guanylate cyclase C (GC-C) receptor activators, such as ST peptide variants)

L67 ANSWER 4 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:1127349 HCAPLUS  
DOCUMENT NUMBER: 142:74574  
TITLE: Preparation of 1,2,4-triazolylethylamines as modulators of the glucocorticoid receptor  
INVENTOR(S): Robinson, Leslie; Rueter, Jaimie K.; Moree, Wilna J.  
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
SOURCE: PCT Int. Appl., 69 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111015	A1	20041223	WO 2004-US18487	20040611 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004266831	A1	20041230	US 2004-865443	20040610 <--
PRIORITY APPLN. INFO.:			US 2003-477545P	P 20030611
OTHER SOURCE(S):			MARPAT 142:74574	

GI



AB Title compds. I [A, B = cycloalkyl, aryl, heteroaryl; R1 = H, acyl, carboxy, etc.; R2-4 = H, alkyl, heteroalkyl, etc.; R5-6 = H, F, Cl, Br, etc.] are prepared General synthetic procedures are provided for the synthesis of 19 examples, e.g., II. Example compds. are tested in a glucocorticoid receptor binding assay in the range of 0.1 nM to 40  $\mu$ M [no data]. I are glucocorticoid receptor modulators and are useful in treating diseases requiring glucocorticoid receptor agonist or antagonist therapy such as obesity, diabetes, inflammatory and immune disorders.

IC ICM C07D249-08

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63

IT **Intestine, disease**

(**inflammatory**; preparation of 1,2,4-triazolylethylamines as modulators of glucocorticoid receptor)

IT **Inflammation**

**Intestine, disease**

(**ulcerative colitis**; preparation of 1,2,4-triazolylethylamines as modulators of glucocorticoid receptor)

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-78-2, Aspirin 51-21-8, 5-Fluorouracil 51-64-9, Dexamphetamine 52-24-4, Thiotepe 52-53-9, Verapamil 53-03-2, Prednisone 53-86-1, Indomethacin 56-03-1, Biguanide 58-32-2, Dipyridamole 59-05-2, Methotrexate 59-67-6, Niacin, biological studies 67-78-7, Triamcinolone diacetate 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 4205-91-8, Clonidine hydrochloride 5536-17-4, Vidarabine 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 15307-79-6, Diclofenac sodium 15663-27-1, Cisplatin 15687-27-1, Ibuprofen 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 36322-90-4,

Piroxicam 41575-94-4, Carboplatin 42200-33-9, Nadolol 49562-28-9,  
Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine  
56180-94-0, Acarbose 59277-89-3, Aciclovir 62571-86-2,  
Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5,  
Lovastatin 75847-73-3, Enalapril 76547-98-3,  
Lisinopril 79217-60-0, Cyclosporin 79902-63-9, Simvastatin  
80830-42-8, Fentiapril 81093-37-0, Pravastatin 82410-32-0, Ganciclovir  
85441-61-8, Quinapril 86541-75-5, Benazepril  
87333-19-5, Ramipril 93479-97-1, Glimepiride 93957-54-1,  
Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7,  
Troglitazone 98048-97-6, Fosinopril 103775-10-6,  
Moexipril 104987-11-3, FK-506 105816-04-4, Nateglinide 106650-56-0,  
Sibutramine 111025-46-8, Pioglitazone 113665-84-2, Clopidogrel  
114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5,  
Atorvastatin 135062-02-1, Repaglinide 136470-78-5, Abacavir  
137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC2993  
143443-90-7, Ifetroban 144288-97-1, TS-962 145599-86-6, Cerivastatin  
147511-69-1, Pitavastatin 152755-31-2, LY295427 159183-92-3, L750355  
160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 162011-90-7,  
Rofecoxib 166518-60-1, Avasimibe 167305-00-2, Omapatrilat  
169319-62-4, CGS30440 169590-42-5, Celecoxib 170861-63-9, JTT-501  
176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel  
196808-45-4, GI-262570 199113-98-9, NN-2344 199914-96-0, YM-440  
213252-19-8, KRP297 244081-42-3, AJ9677 251572-86-8, P32/98  
282526-98-1 335149-08-1, L 895645 335149-14-9, R 119702 335149-15-0,  
KAD 1129 335149-17-2, ARHO 39242 335149-19-4 335149-23-0, NVP-DPP  
728A 335149-25-2, CP 331648 430433-17-3, Glipyrizide  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(combination pharmaceutical; preparation of 1,2,4-triazolyethylamines as  
modulators of glucocorticoid receptor)

IT 9001-62-1, Lipase 9015-82-1, ACE 9027-63-8 9028-35-7  
9033-06-1, Glucosidase 9077-14-9, Squalene synthetase

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(inhibitor, combination pharmaceutical; preparation of  
1,2,4-triazolyethylamines as modulators of glucocorticoid receptor)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 5 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1124594 HCAPLUS

DOCUMENT NUMBER: 142:79882

TITLE: Non-steroidal compound modulators of the  
glucocorticoid receptor and therapeutic uses for  
glucocorticoid receptor agonist or antagonist  
dependent diseases .

INVENTOR(S): Hadida-Ruah, Sara Sabine; He, Xiaohui; Nagasawa,  
Johnny Yasuo

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 75 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

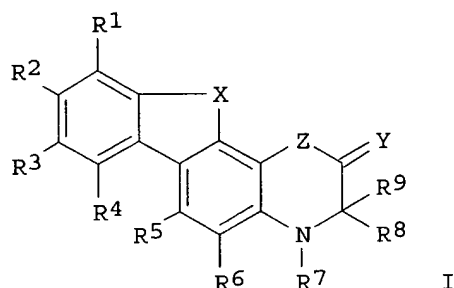
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004110385 A2 20041223 WO 2004-US18677 20040611 <--  
 WO 2004110385 A3 20050127

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
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 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,  
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,  
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 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
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 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG

US 2004266758 A1 20041230 US 2004-865444 20040610 <--  
 PRIORITY APPLN. INFO.: US 2003-477574P P 20030611  
 OTHER SOURCE(S): MARPAT 142:79882  
 GI



AB The present invention relates to new non-steroidal compds. which are glucocorticoid receptor (GR) modulators (that is agonists and antagonists) and thus are useful in treating diseases requiring glucocorticoid receptor agonist or antagonist therapy such as obesity, diabetes and inflammatory or immune associated diseases, and to a method for using such compds. to treat these and related diseases. Specifically, the novel non-steroidal compds. have the structure as formula (I), wherein R1 through R6 are independently (i) hydrogen, F, Cl, Br, I, NO<sub>2</sub>, CN, or OR<sub>10</sub>, etc, (ii) C1-6-alkyl, C3-8-cycloalkyl, or C2-6-alkenyl, etc; R7 is hydrogen, C1-6-alkyl, or C3-8-cycloalkyl, etc; R8 and R9 are independently hydrogen, C1-6-alkyl, or C3-8-cycloalkyl, etc; Y is O, S, or NR<sub>14</sub>; Z is O, S, S(O), S(O)<sub>2</sub>, or NR<sub>15</sub>; and X is OCR<sub>16</sub>R<sub>17</sub>, SCR<sub>16</sub>R<sub>17</sub>, S(O)CR<sub>16</sub>R<sub>17</sub>, etc.

IC ICM A61K

CC 63-5 (Pharmaceuticals)

IT Intestine, disease

(inflammatory; non-steroidal compound modulators of glucocorticoid receptor and therapeutic uses for glucocorticoid receptor agonist or antagonist-dependent diseases)

IT 5-HT reuptake inhibitors

Addison's disease

Allergy

Anti-inflammatory agents

Antibiotics

Antidepressants

Antidiabetic agents

Antihypertensives

Antiobesity agents

Antitumor agents  
 Antiviral agents  
 Appetite depressants  
 Arteriosclerosis  
 Asthma  
 Atherosclerosis  
 Autoimmune disease  
 Behcet's syndrome  
 Blood, disease  
 Calcium channel blockers  
     **Celiac disease**  
 Connective tissue, disease  
 Dermatomyositis  
 Digestive tract, disease  
 Eczema  
 Endocrine system, disease  
 Eye, disease  
 Fungicides  
 Graves' disease  
 Hay fever  
 Hepatitis  
 Hypolipemic agents  
 Immunosuppressants  
 Leukemia  
 Lymphoma  
 Multiple sclerosis  
 Myasthenia gravis  
 Obesity  
 Platelet aggregation inhibitors  
 Psoriasis  
 Rheumatic diseases  
 Rheumatoid arthritis  
 Seborrhea  
 Sepsis  
 Sjogren's syndrome  
 Transplant rejection  
 Urticaria  
     (non-steroidal compound modulators of glucocorticoid receptor and  
     therapeutic uses for glucocorticoid receptor agonist or  
     antagonist-dependent diseases)

IT **Inflammation**    **Intestine, disease**

    (**ulcerative colitis**; non-steroidal compound  
     modulators of glucocorticoid receptor and therapeutic uses for  
     glucocorticoid receptor agonist or antagonist-dependent diseases)

IT 9001-62-1, Lipase 9015-82-1, **Angiotensin-converting**  
 enzyme 9027-63-8, ACAT 9029-60-1, Lipoxigenase 82707-54-8, Neutral  
 endopeptidase

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (**inhibitor**; non-steroidal compound modulators of glucocorticoid  
     receptor and therapeutic uses for glucocorticoid receptor agonist or  
     **antagonist**-dependent diseases)

IT 50-18-0, Cyclophosphamide 50-78-2, Aspirin 51-21-8, 5-Fluorouracil  
 51-64-9, Dexamphetamine 52-24-4, Thiotepe 52-53-9, Verapamil  
 56-03-1, Biguanide 58-32-2, Dipyridamole 59-05-2, Methotrexate  
 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8,  
 Phentermine 446-86-6 483-60-3 525-66-6, Propranolol 637-07-0,  
 Clofibrate 657-24-9, Metformin 943-45-3D, Fibrin acid, derivative  
 4205-91-8 7772-99-8, Tin II chloride, biological studies 10238-21-8,

Glyburide 14838-15-4, Phenylpropanolamine 15663-27-1, Cisplatin 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 41575-94-4, Carboplatin 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 62571-86-2, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79217-60-0, Cyclosporin 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 89149-10-0, Deoxyspergualin 89750-14-1, Glucagon-like peptide-1 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 98048-97-6, Fosinopril 103775-10-6, Moexipril 104987-11-3, FK 506 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC2993 143443-90-7, Ifetroban 144288-97-1, TS 962 145599-86-6, Cerivastatin 147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, CGS30440 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4 199113-98-9, NN 2344 199914-96-0, YM 440 213252-19-8, KRP297 244081-42-3, AJ9677 251572-86-8, P 32/98 282526-98-1 287714-41-4 335149-08-1, L 895645 335149-14-9, R 119702 335149-15-0, KAD 1129 335149-17-2, ARHO 39242 335149-19-4 335149-23-0, NVP-DPP 728A 335149-25-2, CP 331648 430433-17-3, Glipyrside 444069-80-1, Axokine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(non-steroidal compound modulators of glucocorticoid receptor and  
therapeutic uses for glucocorticoid receptor agonist or  
antagonist-dependent diseases)

L67 ANSWER 6 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1124587 HCAPLUS  
DOCUMENT NUMBER: 142:69188  
TITLE: Combination therapy for the treatment of diabetes  
INVENTOR(S): Erondy, Ngozi E.; Fong, Tung M.; MacNeil, Douglas J.;  
Van Der Ploeg, Leonardus H. T.; Kanatani, Akio  
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Banyu Pharmaceutical Co., Ltd.  
SOURCE: PCT Int. Appl., 109 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110375	A2	20041223	WO 2004-US17291	20040602 <--
WO 2004110375	A3	20050512		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
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 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
 SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-476388P

P 20030606

OTHER SOURCE(S):

MARPAT 142:69188

AB The present invention relates to compns. comprising an anti-obesity agent and an anti-diabetic agent useful for the treatment of diabetes, diabetes associated with obesity and diabetes-related disorders. The present invention further relates to methods of treating or preventing obesity, and obesity-related disorders, in a subject in need thereof by administering a composition of the present invention. The present invention further provides for pharmaceutical compns., medicaments, and kits useful in carrying out these methods.

IC ICM A61K

CC 1-10 (Pharmacology)

Section cross-reference(s): 2

IT **Intestine, disease**

(**inflammatory**; combination therapy of diabetes and diabetes-related disorders using antiobesity agent and antidiabetic agent and other agents)

IT **Inflammation**

**Intestine, disease**

(**ulcerative colitis**; combination therapy of diabetes and diabetes-related disorders using antiobesity agent and antidiabetic agent and other agents)

IT 51-64-9, Dextroamphetamine 52-01-7, Spironolactone 52-53-9, Verapamil 54-31-9, Furosemide 58-54-8, Ethacrynic acid 58-93-5, Hydrochlorothiazide 58-94-6, Chlorothiazide 58-94-6D, Thiazide, derivs. 59-67-6, Niacin, biological studies 77-36-1, Chlorthalidone 83-46-5,  $\beta$ -Sitosterol 86-54-4, Hydralazine 90-84-6, Diethylpropion 100-55-0, Nicotinyl alcohol 120-97-8, Dichlorophenamide 122-09-8, Phentermine 134-49-6, Phenmetrazine 135-09-1, Hydroflumethiazide 156-08-1, Benzphetamine 156-34-3, Levamfetamine 300-62-9, Amphetamine 396-01-0, Triamterene 434-43-5, Pentorex 457-87-4, N-Ethylamphetamine 458-24-2, Fenfluramine 461-78-9, Chlorphentermine 525-66-6, Propranolol 532-52-5, Cyclexedrine 537-46-2, Methamphetamine 634-03-7, Phendimetrazine 637-07-0, Clofibrate 720-76-3, Fluminorex 943-45-3D, Fibric acid, derivs. 2207-50-3, Aminorex 2609-46-3, Amiloride 3239-44-9, Dexfenfluramine 3876-10-6, Clominorex 3930-20-9, Sotalol 4205-90-7, Clonidine 4378-36-3, Fenbutrazate 5051-62-7, Guanabenz 8075-95-4, Atromid 9004-10-8, Insulin, biological studies 9004-54-0D, Dextran, crosslinked, dialkylaminoalkyl derivs., biological studies 9028-35-7, HMG-CoA reductase 10238-21-8, Glyburide 10389-73-8, Clortermine 11041-12-6, Cholestyramine 13364-32-4, Clobenzorex 13445-60-8, Furfurylmethylamphetamine 13523-86-9, Pindolol 13862-07-2, Diphemethoxidine 14261-75-7, Cloforex 14838-15-4, Phenylpropanolamine 15221-81-5, Fludorex 15351-09-4, Metamfepramone 16397-28-7, Fenproporex 16662-47-8, Gallopamil 17243-57-1, Mefenorex 19216-56-9, Prazosin 21829-25-4, Nifedipine 22232-71-9, Mazindol 23288-49-5, Probucol 24558-01-8, Levophacetoperane 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 26839-75-8, Timolol 26844-12-2, Indoramin 28395-03-1, Bumetanide 29122-68-7, Atenolol 31036-80-3, Lofexidine 31428-61-2, Tiamenidine 31637-97-5, Etofibrate 34661-75-1, Urapidil 34887-52-0, Fenisorex 35795-16-5, Trimazosin 36393-56-3, Norpseudoephedrine 37296-80-3, Colestid 37517-30-9, Acebutolol 38304-91-5, Minoxidil 38363-40-5, Penbutolol 39562-70-4, Nitrendipine

41859-67-0 42017-89-0, Fenofibric acid 42200-33-9, Nadolol  
 42399-41-7, Diltiazem 49562-28-9, Tricor 50925-79-6, Colestipol  
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 56980-93-9, Celiprolol 57149-07-2, Naftopidil 59170-23-9, Bevantolol  
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 Captopril 62658-63-3, Bopindolol 63590-64-7, Terazosin 63659-18-7,  
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 Nimodipine 66722-44-9, Bisoprolol 68291-97-4, Zonisamide 68377-92-4,  
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**83435-66-9**, Delapril **83647-97-6**, Spirapril 83688-84-0,  
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**85441-61-8** **86541-75-5**, Benazepril 86780-90-7,  
 Aranidipine **87333-19-5**, Ramipril **87679-37-6**,  
 Trandolapril 88150-42-9, Amlodipine **88768-40-5**, Cilazapril  
 89226-50-6, Manidipine **89371-37-9**, Imidapril 93957-54-1,  
 Fluvastatin 94739-29-4, Lemildipine 97240-79-4, Topiramate  
**98048-97-6**, Fosinopril 99522-79-9, Pranidipine 99759-19-0,  
 Tiqueside 100427-26-7, Lercanidipine **103775-10-6**, Moexipril  
 103890-78-4, Lacidipine 104713-75-9, Barnidipine 105979-17-7,  
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 Losartan 118457-14-0, Nebivolol 122320-73-4, Rosiglitazone  
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 138402-11-6, Irbesartan 139158-30-8 139481-59-7, Candesartan  
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 169494-85-3D, Leptin, derivs. 180384-57-0, Tezosentan 182815-43-6,  
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 202340-45-2, Eflucimibe 211513-37-0, JTT 705 221564-97-2, BM 170744  
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 581789-89-1 581789-95-9 581789-99-3 581791-51-7 581791-55-1  
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 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(combination therapy of diabetes and diabetes-related disorders using  
 antiobesity agent and antidiabetic agent and other agents)

L67 ANSWER 7 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:995933 HCAPLUS

DOCUMENT NUMBER: 141:424343

TITLE: Preparation of nitrosated and nitrosylated compounds for use in pharmaceutical compositions a nitric oxide (NO) donors

INVENTOR(S): Earl, Richard A.; Garvey, David S.; Gaston, Ricky D.; Lin, Chia-En; Ranatunge, Ramani R.; Richardson, Stewart K.; Stevenson, Cheri A.

PATENT ASSIGNEE(S): Nitromed, Inc., USA

SOURCE: PCT Int. Appl., 181 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098538	A2	20041118	WO 2004-US7943	20040315 <--
WO 2004098538	A3	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

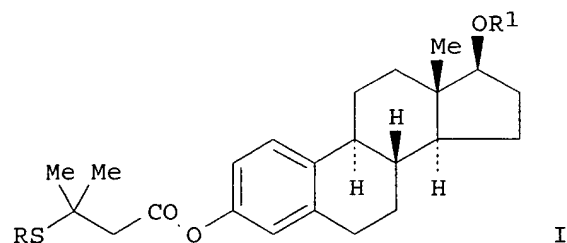
PRIORITY APPLN. INFO.:

US 2003-453963P P 20030313

US 2003-482134P P 20030625

OTHER SOURCE(S): MARPAT 141:424343

GI



AB Nitroso and nitrosyl derivs. of therapeutic agents, such as R-SNO, R-ONO, R-ONO2 [R = antithrombogenic agent, thrombolytic agent, fibrinolytic agent, vasospasm inhibitor, potassium channel blocker, calcium channel blocker, antihypertensive agent, antimicrobial agent, antibiotic, platelet reducing agent, antimitotic agent, antiproliferative agent, microtubule inhibitor, antisecretory agent, remodeling inhibitor, antisense nucleotide, anticancer chemotherapeutic agent, steroid, nonsteroidal antiinflammatory agent, selective COX-2 inhibitor, immunosuppressive agent, growth

factor **antagonist** or antibody, dopamine agonist, radiotherapeutic agent, heavy metal functioning as a radioplaque agent, biol. agent, aldosterone **antagonist**,  $\alpha$ -adrenergic receptor **antagonist**, **angiotensin II antagonist**,  $\beta$ -adrenergic agonist, antihyperlipidemic drug, **angiotensin converting enzyme (ACE) inhibitor**, antioxidant,  $\beta$ -adrenergic **antagonist**, endothelin **antagonist**, neutral endopeptidase **inhibitor**, renin **inhibitor**, free radical scavenger, iron chelator, sex hormone, antipolymerase, antiviral agent, photodynamic therapy agent, antibody targeted therapy agent, gene therapy agent, etc.], were prepared for therapeutic use. The compds. and compns. of this invention can also be bound to a matrix. These nitroso- and nitro-compds. are claimed for use in treating cardiovascular diseases, for inhibiting platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating pathol. conditions resulting from abnormal cell proliferation; transplantation rejections, autoimmune, inflammatory, proliferative, hyperproliferative or vascular diseases; for reducing scar tissue or for inhibiting wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis by administering at least one compound of the invention that is optionally nitrosated and/or nitrosylated, in combination with nitric oxide donors that are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions. The compds. of this invention are preferably estradiol compds., troglitazone compds., tranilast compds., retinoic acid compds., resveratrol compds., mycophenolic acid compds., acid compds., anthracenone compds. and trapidil compds. The cardiovascular diseases for treatment include restenosis, coronary artery disease, atherosclerosis, atherogenesis, cerebrovascular disease, angina, ischemic disease, congestive heart failure or pulmonary edema associated with acute myocardial infarction, aneurysm, thrombosis, hypertension, platelet adhesion, platelet aggregation, smooth muscle cell proliferation, a vascular or non-vascular complication associated with the use of a medical device, wounds associated with the use of a medical device, pulmonary thromboembolism, cerebral thromboembolism, thrombophlebitis, thrombocytopenia or a bleeding disorder. The autoimmune diseases for treatment include a pathol. condition resulting from abnormal cell proliferation, polycystic kidney disease, an inflammatory disease, for preserving an organ and/or a tissue or for inhibiting wound contraction in a patient. The pathol. conditions resulting from abnormal cell proliferation include is a cancer, a Kaposi's sarcoma, a cholangiocarcinoma, a choriocarcinoma, a neblastoma, a Wilm's tumor, Hodgkin's disease, a melanoma, multiple myelomas, a chronic lymphocytic leukemia or an acute or chronic granulocytic lymphoma. The inflammatory diseases for treatment include rheumatoid arthritis, an inflammatory skin disease, restenosis, multiple sclerosis, a surgical adhesion, tuberculosis, a graft rejection, an inflammatory lung disease, an **inflammatory bowel** disease, an inflammatory disease that affects or causes obstruction of a body passageway, an inflammation of the eye, an inflammation of the nose, an inflammation of the throat or a neovascular diseases of the eye. Thus, S-mono- and O,S-dinitroso- $\beta$ -estradiol derivs. I (R = NO, R1 = H, NO) were prepared via an esterification reaction of  $\beta$ -estradiol with 3-methyl-3-(2,4,6-trimethoxyphenylmethylthio)butyric acid using EDAP and DMAP in DMF to form mono-ester I [R = CH<sub>2</sub>C<sub>6</sub>H<sub>2</sub>-2,4,6-(OMe)<sub>3</sub>, R1 = H], cleavage of the trimethoxybenzyl S-protecting group of the mono-ester using L-cysteine and TFA in CH<sub>2</sub>Cl<sub>2</sub> to give thiol I (R = R1 = H), and finally, treatment of the thiol with Bu nitrite in CH<sub>2</sub>Cl<sub>2</sub> to form the desired S-mono- and O,S-dinitroso- $\beta$ -estradiol derivs. The prepared compds. were assayed

for suppression of proliferation of human coronary artery smooth muscle cells.

IC ICM A61K

CC 32-3 (Steroids)

Section cross-reference(s): 1, 25, 28, 30, 63

L67 ANSWER 8 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:817878 HCAPLUS

DOCUMENT NUMBER: 141:332038

TITLE: Bicyclic compounds, particularly N-[(butyloxy)carbonyl]-3-[4-[(substituted-amino)methyl]phenyl]-5-isobutylthiophene-2-sulfonamides, useful as angiotensin II (AT2 receptor) agonists, and their uses, pharmaceutical formulations, preparation, and intermediates

INVENTOR(S): Hallberg, Anders; Alterman, Mathias

PATENT ASSIGNEE(S): Vicore Pharma AB, Swed.; McNeeney, Stephen Phillip

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

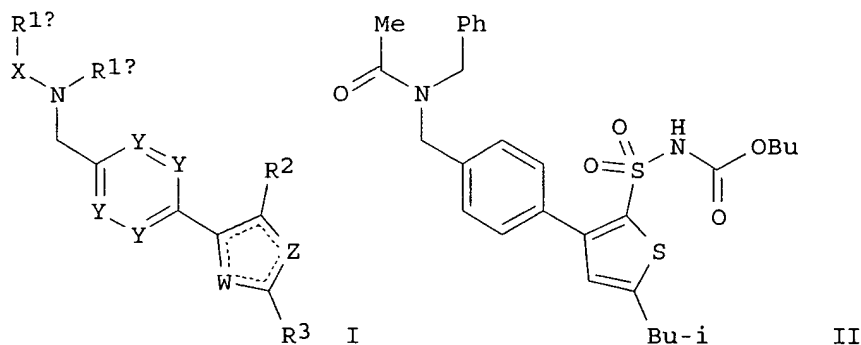
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085420	A1	20041007	WO 2003-GB1251	20030324 <--
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW</p> <p>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p>				
PRIORITY APPLN. INFO.:			WO 2003-GB1251	20030324
OTHER SOURCE(S):			MARPAT 141:332038	

GI



AB Title compds. I and their pharmaceutically-acceptable salts are provided [wherein: X = O, CO, SO<sub>2</sub>; R1a, R1b = H, alkyl, alkoxyalkyl, Ar1, Het1,



alkyl-Het2, alkoxy-Ar3, alkoxy-Het3; or when X = CO then R1a may also be alkoxy or -O-Ar4; Ar1-Ar4 = (independently) (un)substituted C6-10 aryl; Het1-Het3 = (independently) (un)substituted 4- to 12-membered N/O/S heterocycle; Y = (independently) CH or CF; Z = CH, O, S, N, or CH:CH; W = CH, O, S, or N; R2 = SO<sub>2</sub>NHCOR<sub>4</sub>, SO<sub>2</sub>NHSO<sub>2</sub>R<sub>4</sub>, or CONHSO<sub>2</sub>R<sub>4</sub>; or when Z = CH:CH then also R2 = NHSO<sub>2</sub>NHCOR<sub>5</sub> or NHCONHSO<sub>2</sub>R<sub>5</sub>; R3 = alkyl, alkoxy, or alkoxyalkyl; R4 = alkyl, alkoxy, alkoxyalkyl, or (di)alkylamino; R5 = alkyl; provided (1) that Z ≠ W, (2) that W = CH or N when Z = CH:CH, and (3) that, except when Z = CH:CH and W = CH, then if Z or W = CH, then the other = O or S]. I and salts are useful as selective agonists of the AT<sub>2</sub> receptor. As such, they are useful for treatment of a wide variety of conditions, and thus, in particular, in the treatment of (inter alia) gastrointestinal conditions, such as dyspepsia, IBS and MOF, and cardiovascular disorders. Prepns. of 15 compds. I are described. For instance, amidation of thiophene-2-sulfonyl chloride with tert-butylamine, followed by lithiation with BuLi and alkylation with 1-iodo-2-methylpropane, gave 5-isobutyl-N-tert-butylthiophene-2-sulfonamide. This compound underwent a sequence of lithiation in the 3-position with BuLi, boronation with B(OPr-iso)<sub>3</sub>, and Pd(OAc)<sub>2</sub>/PPh<sub>3</sub>-catalyzed coupling with 4-bromobenzaldehyde, to give 3-(4-formylphenyl)-5-isobutyl-N-tert-butylthiophene-2-sulfonamide. This key aldehyde intermediate underwent reductive amination with various amines and NaBH<sub>4</sub>, followed by N-acylation with acid chlorides or alkyl chloroformates, deprotection of the sulfonamide with TFA and anisole, and N-acylation of the sulfonamide N with n-Bu chloroformate. Using PhCH<sub>2</sub>NH<sub>2</sub> and AcCl in the last steps, example compound II was prepared. The example compds. bound preferentially to porcine myometrial membrane AT<sub>2</sub> receptors, showing K<sub>i</sub> less than 50 nM, whereas they bound to rat liver membrane AT<sub>1</sub> receptors with K<sub>i</sub> = 1 μM or greater. In a duodenal mucosal alkaline secretion assay in anesthetized rats, the example compds. markedly stimulated mucosal alkalization (no data); this effect was blocked by coadministration of the selective AT<sub>2</sub> receptor antagonist PD123319.

IC ICM C07D333-34

ICS C07D409-12; C07D333-38; A61K031-381; A61P009-00

CC 27-8 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

IT **Intestine, disease**

(inflammatory, treatment of; preparation of  
(butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as  
angiotensin II (AT<sub>2</sub> receptor) agonists)

IT Angiogenesis

Apoptosis

Asthma

Atherosclerosis

Autoimmune disease

Biliary tract, disease

Cardiovascular system, disease

**Celiac disease**

Central nervous system, disease

Cognitive disorders

Diarrhea

Digestive tract, disease

Dyspepsia

Eating disorders

Eye, disease

Gallbladder, disease

Hepatitis

Hypertension

Hypertrophy

Inflammation  
Ischemia  
Kidney, disease  
Liver, disease  
Multiple organ failure  
Nausea  
Neoplasm  
Obesity  
Preeclampsia  
Psoriasis  
Respiratory system, disease  
Sepsis  
Sjogren's syndrome  
Thirst  
Transplant rejection  
Ulcer  
Vomiting

(treatment of; preparation of (butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as angiotensin II (AT2 receptor) agonists)

IT **Stomach, disease**

(ulcer, treatment of; preparation of (butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as angiotensin II (AT2 receptor) agonists)

IT **Inflammation****Intestine, disease**

(ulcerative colitis, treatment of; preparation of (butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as angiotensin II (AT2 receptor) agonists)

IT 9015-82-1, **Angiotensin converting enzyme**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(therapeutic compns. containing **inhibitors** of; preparation of (butoxycarbonyl)(aminomethylphenyl)isobutylthiophenesulfonamides as **angiotensin** II (AT2 receptor) agonists)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 9 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:817632 HCAPLUS

DOCUMENT NUMBER: 141:307605

TITLE: Pharmaceutical compositions using transition metal chelators for inhibiting metal ion-dependent enzymatic activity, and therapeutic use

INVENTOR(S): Appelbaum, Jerachmiel

PATENT ASSIGNEE(S): Israel

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004084799	A2	20041007	WO 2004-IL279	20040325 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,  
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,  
 TD, TG

## PRIORITY APPLN. INFO.:

IL 2003-155111

A 20030327

AB The invention provides pharmaceutical compns. for inhibiting pathol. functions of metal-dependent metalloproteases, as well as for neutralizing bacterial virulence factors, by employing chelators of transition metals, resulting in reduction in the availability of such metals, or by replacing the key metal ions with different ions. In addition, the invention discloses the use of such metalloprotease inhibitors for the manufacture of a pharmaceutical composition for the prevention or treatment of pathol. conditions influenced by the action of metalloproteases. The invention further discloses methods of treatment or prevention of such conditions.

IC ICM A61K

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

## IT Inflammation

## Intestine, disease

(ulcerative colitis; transition metal chelators for inhibiting metal ion-dependent enzymes, and therapeutic use)

IT 52-67-5, Penicillamine 107-15-3, Ethylenediamine, biological studies  
 111-40-0, Diethylenetriamine 111-41-1 112-24-3, Triethylenetetramine  
 112-57-2 280-57-9, Triethylenediamine 4067-16-7, Pentaethylenhexamine  
 7440-56-4, Germanium, biological studies 7440-56-4D, Germanium, compds.  
 7440-56-4D, Germanium, complexes with TPEN 16858-02-9D, Tpen, derivs.  
 16858-02-9D, TPEN, germanium complexes 21121-06-2, Triethylenetetramine  
 hydrochloride 21121-07-3, Tetraethylenepentamine hydrochloride  
 28631-79-0, Aminoethylpiperazine 57578-49-1, Pentaethylenhexamine  
 hydrochloride 62571-86-2, Captopril

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(transition metal chelators for inhibiting metal ion-dependent enzymes, and therapeutic use)

L67 ANSWER 10 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:681510 HCAPLUS

DOCUMENT NUMBER: 141:200192

TITLE: Methods and compositions using guanylate cyclase C receptor activators for the treatment of gastrointestinal disorders

INVENTOR(S): Currie, Mark G.; Mahajan-Miklos, Shalina

PATENT ASSIGNEE(S): Microbia, Inc., USA

SOURCE: PCT Int. Appl., 93 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069165	A2	20040819	WO 2004-US2390	20040128 <--
WO 2004069165	A3	20050317		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI  
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,  
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,  
MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG  
CA 2514507 AA 20040819 CA 2004-2514507 20040128 <--  
EP 1594517 A2 20051116 EP 2004-706011 20040128  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
PRIORITY APPLN. INFO.: US 2003-443098P P 20030128  
US 2003-471288P P 20030515  
US 2003-519460P P 20031112  
WO 2004-US2390 W 20040128

OTHER SOURCE(S): MARPAT 141:200192

AB The invention discloses compns. and related methods for treating irritable  
bowel syndrome (IBS) and other gastrointestinal disorders and conditions,  
e.g. gastrointestinal motility disorders, functional gastrointestinal  
disorders, gastroesophageal reflux disease (GERD), Crohn's disease,  
**ulcerative colitis, inflammatory bowel**  
disease, functional heartburn, dyspepsia (including functional dyspepsia  
or nonulcer dyspepsia), gastroparesis, chronic intestinal  
pseudo-obstruction (or colonic pseudo-obstruction), and disorders and  
conditions associated with constipation, e.g., constipation associated with use  
of opiate pain killers, post-surgical constipation, and constipation  
associated with neuropathic disorders as well as other conditions and  
disorders using peptides and other agents that activate the guanylate  
cyclase C (GC-C) receptor.

IC ICM A61K

CC 1-9 (Pharmacology)

IT **Intestine, disease**

(**inflammatory**; guanylate cyclase C receptor activators for  
treatment of gastrointestinal disorders)

IT **Inflammation**

**Intestine, disease**

(**ulcerative colitis**; guanylate cyclase C receptor  
activators for treatment of gastrointestinal disorders)

IT .9015-82-1, **Angiotensin-converting enzyme** 9068-52-4,

CGMP Phosphodiesterase 37255-34-8, 5 $\alpha$ -Reductase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**inhibitors**; guanylate cyclase C receptor activators for  
treatment of gastrointestinal disorders)

L67 ANSWER 11 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:589364 HCAPLUS

DOCUMENT NUMBER: 141:117196

TITLE: Nitrosated and nitrosylated rapamycin compounds,  
compositions and methods of use

INVENTOR(S): Garvey, David S.

PATENT ASSIGNEE(S): Nitromed, Inc., USA

SOURCE: PCT Int. Appl., 89 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060283	A2	20040722	WO 2003-US39562	20031215 <--

WO 2004060283 A3 20050324

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,  
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,  
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,  
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,  
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005209266 A1 20050922 US 2005-135308 20050524

PRIORITY APPLN. INFO.: US 2002-433595P P 20021216

US 2003-513215P P 20031023

WO 2003-US39562 A1 20031215

OTHER SOURCE(S): MARPAT 141:117196

AB The invention describes novel nitrosated and/or nitrosylated rapamycin compds., and novel compns. comprising at least one nitrosated and/or nitrosylated rapamycin compound, and, optionally, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one therapeutic agent. The invention also provides novel compns. comprising at least one rapamycin compound and at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one therapeutic agent. The compds. and compns. of the invention can also be bound to a matrix. The invention also provides methods for treating and/or preventing cardiovascular diseases, for the prevention of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating and/or preventing pathol. conditions resulting from abnormal cell proliferation; transplantation rejections; autoimmune, inflammatory, proliferative, hyperproliferative or vascular diseases; for reducing scar tissue or for inhibiting wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis by administering nitrosated and/or nitrosylated rapamycin compds. or rapamycin compds. in combination with nitric oxide donors that are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions.

IC ICM A61K

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

IT Intestine, disease

(inflammatory; nitrosated and nitrosylated rapamycin compds.

for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

IT 9015-82-1, Angiotensin converting enzyme 9015-94-5,

Renin, biological studies 82707-54-8, Neutral endopeptidase

329900-75-6, Cyclooxygenase 2 433935-36-5, Polymerase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; nitrosated and nitrosylated rapamycin compds.

for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

L67 ANSWER 12 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:392331 HCAPLUS

DOCUMENT NUMBER: 140:406798

TITLE: Preparation of benzoxepinopyridines as HMG-CoA

reductase inhibitors  
 INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S.  
 Ser. No. 875,155, abandoned.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004092573	A1	20040513	US 2003-602752	20030624 <--
US 6812345	B2	20041102		
US 2002013334	A1	20020131	US 2001-875155	20010606 <--
PRIORITY APPLN. INFO.:			US 2000-211595P	P 20000615
			US 2001-875155	B2 20010606
OTHER SOURCE(S):	MARPAT 140:406798			
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [X = O, S, SO, SO<sub>2</sub>, NR<sub>7</sub>; Z = HOCHCH<sub>2</sub>CH(OH)CH<sub>2</sub>CO<sub>2</sub>R<sub>3</sub>, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R<sub>1</sub>, R<sub>2</sub> = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R<sub>3</sub> = H, alkyl, metal ion; R<sub>4</sub> = H, halo, CF<sub>3</sub>, etc.; R<sub>7</sub> = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R<sub>9</sub>, R<sub>10</sub> = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). A multistep synthesis of II is reported.

IC ICM A61K031-40

INCL 514423000

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT **Stomach, disease**

(ulcer, treatment; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-01-7, Spironolactone  
 52-53-9, Verapamil 54-31-9, Furosemide 58-32-2, Dipyrindamole  
 58-93-5, Hydrochlorothiazide 59-67-6, Niacin, biological studies  
 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol  
 564-25-0, Doxycycline 637-07-0, Clofibrate 657-24-9, Metformin  
 1684-40-8, Tacrine hydrochloride 3416-24-8, Glucosamine 4205-91-8,  
 Clonidine hydrochloride 9004-61-9, Hyaluronic acid 9007-28-7,  
 Chondroitin sulfate 10118-90-8, Minocycline 10238-21-8, Glyburide  
 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride  
 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol  
 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 29094-61-9, Glipizide  
 29122-68-7, Atenolol 42200-33-9, Nadolol 49562-28-9, Fenofibrate  
 55142-85-3, Ticlopidine 56180-94-0, Acarbose 56211-40-6, Torasemide  
 62571-86-2, Captopril 68475-42-3, Anagrelide 72432-03-2,

Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 98048-97-6, Fosinopril 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 113665-84-2, Clopidogrel 114798-26-4, Losartan 120014-06-4, Donepezil 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC2993 143443-90-7, Ifetroban 143653-53-6, Abciximab 144288-97-1, TS 962 144494-65-5, Tirofiban 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 152755-31-2, LY295427 159183-92-3, LY315902 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 162011-90-7, Vioxx 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, CGS 30440 169590-42-5, Celebrex 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 188627-80-7, Eptifibatide 196808-45-4, GI-262570 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 246852-12-0, Amlodipine mesylate 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4, Rosuvastatin 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, AR-HO39242 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipryride 430433-43-5, CP644673 444069-80-1, Axokine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 13 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:80450 HCAPLUS

DOCUMENT NUMBER: 140:145835

TITLE: Preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of the glucocorticoid receptor

INVENTOR(S): Vaccaro, Wayne; Yang, Bingwei Vera; Kim, Soong-hoon; Huynh, Tram; Tortolani, David R.; Leavitt, Kenneth J.; Li, Wenying; Doweiko, Arthur M.; Chen, Xiao-tao; Doweiko, Lidia

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; et al.

SOURCE: PCT Int. Appl., 265 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

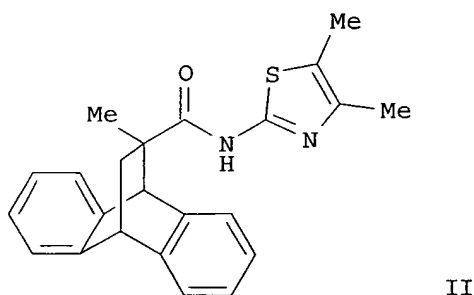
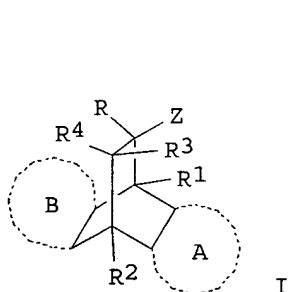
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009017	A2	20040129	WO 2003-US22300	20030717 <--
WO 2004009017	A3	20040708		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,  
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,  
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 US 2004132758 A1 20040708 US 2003-621909 20030717 <--  
 EP 1534273 A2 20050601 EP 2003-765638 20030717  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 NO 2005000074 A 20050309 NO 2005-74 20050106  
 US 2005171136 A1 20050804 US 2005-85347 20050321  
 PRIORITY APPLN. INFO.: US 2002-396877P P 20020718  
 US 2003-621909 A1 20030717  
 WO 2003-US22300 W 20030717  
 OTHER SOURCE(S): MARPAT 140:145835  
 GI



AB Title compds. I [R-R4 = H, alk(en/yn)yl, alkoxy, aryl, etc.; Z = carboxamido, alkylamino, etc.] are prepared For instance, 2-amino-4,5-dimethylthiazole is coupled to the acid derived from the cycloaddn. of methacrylic acid and anthracene (CH3CN, EDCI, Et3N, HOAt, 18 h) to give II. I are glucocorticoid receptor modulators which are useful in treating diseases requiring glucocorticoid receptor agonist or antagonist therapy such as obesity, diabetes, inflammatory and immune disorders.

IC ICM A61K

CC 24-7 (Alicyclic Compounds)  
 Section cross-reference(s): 1, 63

IT **Intestine, disease**  
 (inflammatory; preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid receptor)

IT Addison's disease  
 Adrenal gland, disease  
 Anemia (disease)  
 Antiarthritics  
 Antiasthmatics  
 Antirheumatic agents  
 Asthma  
 Atherosclerosis



Autoimmune disease  
 Behcet's syndrome  
 Blood, disease  
     **Celiac disease**  
 Connective tissue, disease  
 Dermatitis  
 Dermatomyositis  
 Diabetes insipidus  
 Diabetes mellitus  
 Digestive tract, disease  
 Eczema  
 Endocrine system, disease  
 Eye, disease  
 Gout  
 Graves' disease  
 Hay fever  
 Hepatitis  
 Human  
 Inflammation  
 Leukemia  
 Lymphoma  
 Multiple sclerosis  
 Myasthenia gravis  
 Neoplasm  
 Obesity  
 Osteoarthritis  
 Psoriasis  
 Respiratory system, disease  
 Rheumatic diseases  
 Rheumatoid arthritis  
 Seborrhea  
 Sepsis  
 Sjogren's syndrome  
 Skin, disease  
 Transplant rejection  
     (preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as  
     modulators of glucocorticoid receptor)

IT **Inflammation**

**Intestine, disease**

        (ulcerative colitis; preparation of dibenzofused  
         bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid  
         receptor)

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-23-7,  
 Hydrocortisone 50-78-2, Aspirin 51-21-8, 5-Fluorouracil 51-64-9,  
 Dexamphetamine 52-24-4, Thiotepa 52-53-9, Verapamil 53-03-2,  
 Prednisone 53-86-1, Indomethacin 58-32-2, Dipyridamole 59-05-2,  
 Methotrexate 59-67-6, Niacin, biological studies 67-78-7,  
 Triamcinolone diacetate 94-20-2, Chlorpropamide 122-09-8, Phentermine  
 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin  
 943-45-3D, Fibric acid, derivs. 4205-91-8, Clonidine monohydrochloride  
 5536-17-4, Vidarabine 10238-21-8, Glyburide 14838-15-4,  
 Phenylpropanolamine 15307-79-6, Diclofenac sodium 15663-27-1,  
 Cisplatin 15687-27-1, Ibuprofen 19237-84-4, Prazosin hydrochloride  
 21187-98-4, Glucalazide 21829-25-4, Nifedipine 22071-15-4, Ketoprofen  
 22204-53-1, Naproxen 22232-71-9, Mazindol 25812-30-0, Gemfibrozil  
 29094-61-9, Glipizide 36322-90-4, Piroxicam 41575-94-4, Carboplatin  
 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide  
 55142-85-3, Ticlopidine 56180-94-0, Acarbose 59277-89-3, Aciclovir  
 62571-86-2, Captopril 72432-03-2, Miglitol 72956-09-3,

Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79217-60-0, Cyclosporin 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 82410-32-0, Ganciclovir 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 98048-97-6, Fosinopril 103775-10-6, Moexipril 104987-11-3, FK-506 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 136470-78-5, Abacavir 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993 143443-90-7, Ifetroban 144288-97-1, TS-962 145599-86-6, Cerivastatin 147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 162011-90-7, Rofecoxib 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169590-42-5, Celecoxib 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4, GI 262570 199113-98-9, NN 2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, AR-HO39242 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipryide 444069-80-1, Axokine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (combination pharmaceutical; preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid receptor)

IT 9015-82-1, **Angiotensin-converting enzyme**  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inhibitors, combination pharmaceutical; preparation of dibenzofused bicyclo[2.2.2]octane-derived amides as modulators of glucocorticoid receptor)

L67 ANSWER 14 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:60341 HCAPLUS

DOCUMENT NUMBER: 140:117406

TITLE: Liquid dosage compositions of stable nanoparticulate drugs

INVENTOR(S): Bosch, William H.; Hilborn, Matthew R.; Hovey, Douglas C.; Kline, Laura J.; Lee, Robert W.; Pruitt, John D.; Ryde, Niels P.; Ryde, Tuula A.; Xu, Shuqian

PATENT ASSIGNEE(S): Elan Pharma International, Ltd, Ire.

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 16

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006959	A1	20040122	WO 2003-US22187	20030716 <--
WO 2004006959	C1	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,

PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,  
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 CA 2492488 AA 20040122 CA 2003-2492488 20030716 <--  
 EP 1551457 A1 20050713 EP 2003-764723 20030716  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 JP 2005536512 T2 20051202 JP 2004-521891 20030716  
 PRIORITY APPLN. INFO.: US 2002-396530P P 20020716  
 WO 2003-US22187 W 20030716

AB The present invention relates to liquid dosage compns. of stable  
 nanoparticulate drugs. The liquid dosage compns. of the invention include  
 osmotically active crystal growth inhibitors that stabilize the  
 nanoparticulate active agents against crystal and particle size growth of  
 the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD)  
 comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate  
 0.464% by weight was prepared by milling for 3.8 h under high energy milling  
 conditions. The final mean particle size (by weight) of the drug particles  
 was 161 nm. The concentrated NCD was then diluted with preserved water and  
 glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0%  
 drug.

IC ICM A61K047-02  
 ICS A61K047-10; A61K047-26; A61K009-10; A61K009-14; A61K031-192;  
 A61K031-58

CC 63-6 (Pharmaceuticals)

IT **Intestine, disease**  
 (inflammatory; liquid dosage compns. of stable nanoparticulate  
 drugs)

IT 50-35-1, Thalidomide 50-44-2, Mercaptopurine 50-53-3, Chlorpromazine,  
 biological studies 50-78-2, Acetylsalicylic acid 50-99-7, Glucose,  
 biological studies 52-53-9, Verapamil 56-81-5, Glycerol, biological  
 studies 56-85-9, Glutamine, biological studies 57-09-0,  
 Hexadecyltrimethylammonium bromide 57-11-4, Stearic acid, biological  
 studies 57-48-7, Fructose, biological studies 57-50-1, Sucrose,  
 biological studies 57-55-6, Propylene glycol, biological studies  
 57-88-5, Cholesterol, biological studies 58-32-2, Dipyrindamole  
 59-30-3, Folic acid, biological studies 62-49-7D, Choline, esters  
 63-42-3, Lactose 64-17-5, Ethanol, biological studies 67-45-8,  
 Furazolidone 69-65-8, Mannitol 69-89-6D, Xanthine, derivs. 73-31-4,  
 Melatonin 75-65-0, biological studies 80-74-0, Acetylsulfisoxazole  
 87-99-0, Xylitol 99-20-7, Trehalose 102-71-6, Triethanolamine,  
 biological studies 110-86-1D, Pyridine, quaternized, salts 112-00-5,  
 Lauryltrimethylammonium chloride 123-03-5, CPC 129-03-3,  
 Cyproheptadine 132-17-2, Benztropine mesylate 134-32-7D,  
 1-Naphthylamine, alkyltrimethylammonium salts 139-07-1,  
 Lauryldimethylbenzylammonium chloride 140-72-7, Cetylpyridinium bromide  
 143-67-9, Vinblastine sulfate 148-79-8, Thiabendazole 151-21-3, SDS,  
 biological studies 154-42-7, Thioguanine 288-32-4D, Imidazole,  
 quaternized, salts 303-53-7, Cyclobenzaprine 396-01-0, Triamterene  
 500-92-5, Proguanil 502-65-8, Lycopene 645-05-6, Altretamine  
 846-50-4, Temazepam 1119-94-4, Dodecyltrimethylammonium bromide  
 1119-97-7, Tetradecyltrimethylammonium bromide 1200-22-2, Lipoic acid  
 1327-43-1, Magnesium aluminum silicate 1592-23-0, Calcium Stearate  
 1643-19-2, Tetrabutylammonium bromide 1951-25-3, Amiodarone 1977-10-2,  
 Loxapine 2062-78-4, Pimozide 2082-84-0, Decyltrimethylammonium bromide  
 2609-46-3, Amiloride 3416-24-8, Glucosamine 3458-28-4, Mannose

4205-90-7, Clonidine 4342-03-4, Dacarbazine 5137-55-3, Methyltriethylammonium chloride 5350-41-4, Benzyltrimethylammonium bromide 7173-51-5, Dimethyldidecylammonium chloride 7281-04-1, Lauryldimethylbenzylammonium bromide 7447-40-7, Potassium chloride (KCl), biological studies 7647-14-5, Sodium chloride, biological studies 7786-30-3, Magnesium chloride (MgCl<sub>2</sub>), biological studies 9000-01-5, Gum acacia 9000-30-0D, Guar gum, cationic derivs. 9000-65-1, Tragacanth gum 9001-63-2, Lysozyme 9002-89-5, Poly(vinyl alcohol) 9003-39-8, Polyvinylpyrrolidone 9004-32-4 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hypromellose 9004-67-5, Methyl cellulose 9004-99-3, Polyethylene glycol stearate 9005-32-7, Alginic acid 9007-12-9, Calcitonin 9007-27-6, Chondroitin 9011-14-7, Poly(methyl methacrylate) 9011-14-7D, Poly(methyl methacrylate), hydrolyzed, trimethylammonium salts 9050-04-8, Cellulose, carboxymethyl ether, calcium salt 9050-31-1, Hydroxypropyl methyl cellulose phthalate 10118-90-8, Minocycline 12441-09-7D, Sorbitan, esters 13292-46-1, Rifampin 16679-58-6, Desmopressin 18186-71-5, Dodecyltriethylammonium bromide 24280-93-1 25086-89-9, Vinyl acetate-1-vinyl-2-pyrrolidone copolymer 25301-02-4, Ethylene oxide-formaldehyde-4-(1,1,3,3-Tetramethylbutyl)phenol copolymer 25322-68-3, Polyethylene glycol 25322-68-3D, Polyethylene glycol, phospholipid derivs. 26062-79-3, Poly(diallyldimethylammonium chloride) 27195-16-0, Sucrose distearate 27321-96-6, Polyethylene glycol cholesteryl ether 28228-56-0 28679-24-5, Dodecylbenzyltriethylammonium chloride 28981-97-7, Alprazolam 29094-61-9, Glipizide 29767-20-2, Teniposide 29836-26-8, n-Octyl- $\beta$ -D-glucopyranoside 31431-39-7, Mebendazole 31566-31-1, Glyceryl monostearate 33419-42-0, Etoposide 34911-55-2, Bupropion 36735-22-5, Quazepam 37318-31-3, Sucrose stearate 38443-60-6, Decyltriethylammonium chloride 39809-25-1, Penciclovir 42399-41-7, Diltiazem 51264-14-3, Amsacrine 51569-39-2, Olin 10G 52128-35-5, Trimetrexate 52467-63-7, Tricetylmethylammonium chloride 55008-57-6 55268-75-2, Cefuroxime 55348-40-8, Triton X-200 58846-77-8, n-Decyl  $\beta$ -D-glucopyranoside 59080-45-4, n-Hexyl  $\beta$ -D-glucopyranoside 59122-55-3, n-DoDecyl  $\beta$ -D-glucopyranoside 59277-89-3, Acyclovir 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 69227-93-6, n-DoDecyl  $\beta$ -D-maltoside 69984-73-2, n-Nonyl  $\beta$ -D-glucopyranoside 70458-96-7, Norfloxacin 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72559-06-9, Rifabutin 73590-58-6, Omeprazole 76095-16-4, Enalapril maleate 76420-72-9, Enalaprilat 76824-35-6, Famotidine 78617-12-6, n-Heptyl  $\beta$ -D-glucopyranoside 79617-96-2, Sertraline 79794-75-5, Loratadine 81098-60-4, Cisapride 81103-11-9, Clarithromycin 81409-90-7, Cabergoline 81859-24-7, Polyquat 10 82494-09-5, n-Decyl  $\beta$ -D-maltoside 84449-90-1, Raloxifene 85261-19-4, Nonanoyl-N-methylglucamide 85261-20-7, Decanoyl-N-methylglucamide 85316-98-9 85618-20-8, n-Heptyl  $\beta$ -D-thiogluconopyranoside 85618-21-9, n-Octyl- $\beta$ -D-thiogluconopyranoside 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 87679-37-6, Trandolapril 91161-71-6, Terbinafine 95233-18-4, Atovaquone 97322-87-7, Troglitazone 100286-97-3, Milrinone lactate 101397-87-9, D-Glucitol, 1-deoxy-1-[methyl(1-oxoheptyl)amino]- 103577-45-3, Lansoprazole 104987-11-3, Tacrolimus 106266-06-2, Risperidone 106392-12-5, Pluronic 107397-59-1, Tetronic 150R8 110617-70-4, Poloxamine 113665-84-2, Clopidogrel 115956-12-2, Dolasetron 127666-00-6 127779-20-8, Saquinavir 132539-06-1, Olanzapine 136817-59-9, Delavirdine 138402-11-6, Irbesartan 139481-59-7, Candesartan 139755-83-2, Sildenafil 144034-80-0, Rizatriptan 145599-86-6, Cerivastatin 147059-72-1, Trovafloxacin 159989-65-8,

Nelfinavir mesylate 283158-20-3 329326-68-3, p-  
Isononylphenoxypolyglycidol 503178-50-5 608094-65-1, PEG-vitamin A  
630400-66-7 630400-67-8 634601-99-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(liquid dosage compns. of stable nanoparticulate drugs)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 15 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:41231 HCAPLUS

DOCUMENT NUMBER: 140:111429

TITLE: Preparation of substituted heterocyclic derivatives  
useful as antidiabetic and antiobesity agents

INVENTOR(S): Cheng, Peter T. W.; Chen, Sean; Devasthale, Pratik;  
Ding, Charles Z.; Herpin, Timothy F.; Wu, Shung;  
Zhang, Hao; Wang, Wei; Ye, Xiang-Yang

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 543 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

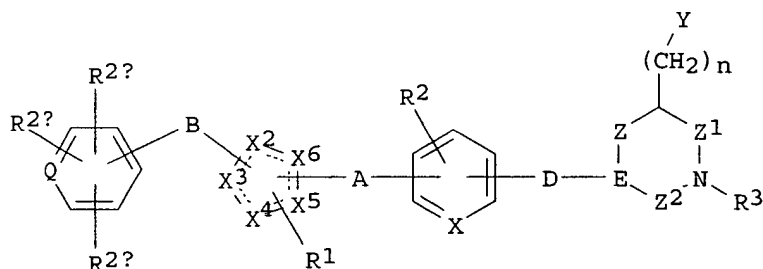
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004665	A2	20040115	WO 2003-US22149	20030702 <--
WO 2004004665	A3	20040325		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
JP 2005536494	T2	20051202	JP 2004-520148	20030702
US 2004063700	A1	20040401	US 2003-616365	20030708 <--
NO 2005000077	A	20050203	NO 2005-77	20050106
PRIORITY APPLN. INFO.:			US 2002-394508P	P 20020709
			WO 2003-US22149	W 20030702

OTHER SOURCE(S): MARPAT 140:111429

GI



AB The title compds. (I) [Z1 = (CH2)q, CO; Z2 = (CH2)p, CO; D = CH, CO, (CH2)m (where m = 0-3; p = 1, 2; q = 0-2); n = 0-2; Q = C, N; A = (CH2)x (where x = 1-5); A = (CH2)x1 (where x1 = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain; or A = -(CH2)x2-O-(CH2)x3- (where X2, X3 = 0 to 5, provided that at least one of x2 and x3 is other than 0); B = a bond or (CH2)x4 (where x4 = 1-5); X = CH, N; X2-X6 = C, N, O, or S and at least one of X2-X6 is C; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halogen, (un)substituted amino; R2a, R2b, R2c = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, etc.; E = CH, N; Z = (CH2)x5 (where x5 is 0, i.e. a single or a double bond, 1, 2), or Z is (CH2)x6 (where x6 = 2-5), where (CH2)x6 includes an alkenyl (C:C) bond embedded within the chain or Z = -(CH2)x7-O-(CH2)x8- (where x7, x8 = 0-4); (CH2)x to (CH2)x8, (CH2)m, (CH2)n, (CH2)p and (CH2)q may be optionally substituted; Y = CO2R4 (where R4 = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR4a)R5 [where R4a = H, a prodrug ester; R5 = alkyl or aryl, or a phosphonic acid of the structure P(O)(OR4a)2]] including all stereoisomers, prodrug esters, and pharmaceutically acceptable salts thereof are prepared These compds., e.g. cis-1-ethoxycarbonyl-4-[3-[2-(2-phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidin-3-ylacetic acid and cis-1-(6-trifluoromethylpyrimidin-2-yl)-4-[3-[2-(2-phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidine-3-carboxylic acid, modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty acid (NEFA) levels, and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia,

hyperinsulinemia,

hyperlipidemia, obesity, atherosclerosis, and related diseases employing such substituted acid derivs. alone or in combination with another antidiabetic agent and/or a hypolipidemic agent and/or other therapeutic agents. Disclosed is a method for treating diabetes, especially Type 2 diabetes, and related diseases such as insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, inflammation, Syndrome X, diabetic complications, dysmetabolic syndrome, atherosclerosis, and related diseases, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I. Also disclosed is a method for treating early malignant lesions (such as ductal carcinoma in situ of the breast and lobular carcinoma in situ of the breast), premalignant lesions including fibroadenoma of the breast and prostatic intraepithelial neoplasia (PIN), liposarcomas and various other epithelial tumors (including breast, prostate, colon, ovarian, gastric and lung), irritable bowel syndrome, Crohn's disease, gastric ulceritis, and osteoporosis and proliferative diseases such as psoriasis, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I.

IC ICM A61K

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT **Stomach, disease**

(gastric ulceritis; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 56-03-1, Biguanide 58-32-2, Dipyrindamole 59-67-6, Niacin, biological studies 94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 4205-91-8, Clonidine monohydrochloride 10238-21-8, Glyburide

14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride  
 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol  
 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol  
 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3,  
 Ticlopidine 56180-94-0, Acarbose 62571-86-2, Captopril  
 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin  
 75847-73-3, Enalapril 76547-98-3, Lisinopril  
 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin  
 85441-61-8, Quinapril 86541-75-5, Benazepril  
 87333-19-5, Ramipril 89750-14-1, Glucagon-like peptide I  
 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat  
 97240-79-4, Topiramate 98048-97-6, Fosinopril  
 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0,  
 Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate  
 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4,  
 Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide  
 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993  
 143443-90-7, Ifetroban 144288-97-1, TS-962 144701-48-4, Telmisartan  
 147511-69-1, Itavastatin 152755-31-2, LY295427 159183-92-3, L750355  
 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 163222-33-1,  
 Ezetimibe 166518-60-1, Avasimibe 167305-00-2, Omapatrilat  
 168273-06-1, Rimonabant 169319-62-4, CGS 30440 170861-63-9, JTT-501  
 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel  
 196808-45-4 199113-98-9, Balaglitazone 199914-96-0, YM-440  
 213252-19-8, KRP297 244081-42-3, AJ9677 251565-85-2, AR-H 039242  
 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4, Visastatin  
 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129  
 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648  
 430433-17-3, Glipyrside 444069-80-1, Axokine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (combination therapy; preparation of substituted heterocyclic derivs. as  
 antidiabetic and antiobesity agents)

L67 ANSWER 16 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:41224 HCAPLUS

DOCUMENT NUMBER: 140:111417

TITLE: Preparation of substituted heterocyclic derivatives  
 useful as antidiabetic and antiobesity agents

INVENTOR(S): Cheng, Peter T. W.; Chen, Sean; Ding, Charles Z.;  
 Herpin, Timothy F.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 160 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004655	A2	20040115	WO 2003-US21331	20030708 <--
WO 2004004655	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

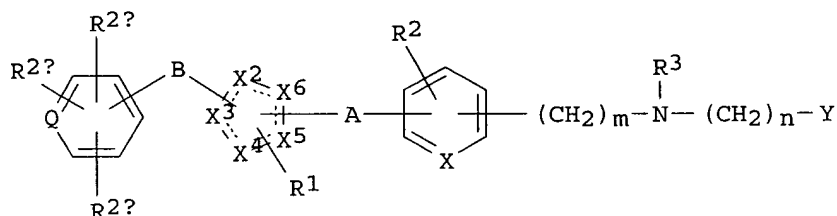
CA 2490972	AA	20040115	CA 2003-2490972	20030708 <--
US 2004063762	A1	20040401	US 2003-616283	20030708 <--
US 6875782	B2	20050405		
EP 1531810	A2	20050525	EP 2003-763345	20030708

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

NO 2004005529	A	20050203	NO 2004-5529	20041217
US 2005119312	A1	20050602	US 2004-16183	20041217

PRIORITY APPLN. INFO.: US 2002-394553P P 20020709  
US 2003-616283 A3 20030708  
WO 2003-US21331 W 20030708

OTHER SOURCE(S): MARPAT 140:111417  
GI



I

AB Compds. having general structure (I) [Q = C, N; A = (un)substituted (CH<sub>2</sub>)<sub>x</sub> (where x = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain, or A = (un)substituted -(CH<sub>2</sub>)<sub>x2</sub>-O-(CH<sub>2</sub>)<sub>x3</sub>- (where x<sub>2</sub>, x<sub>3</sub> = 0-5, provided that at least one of x<sub>2</sub> and x<sub>3</sub> is other than 0); B = a bond, (un)substituted (CH<sub>2</sub>)<sub>x4</sub> (where x<sub>4</sub> = 1-5); X = CH, N; X<sub>2</sub>-X<sub>6</sub> = C, N, O, or S, provided that at least one of X<sub>2</sub>-X<sub>6</sub> is N; and at least one of X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub>, X<sub>5</sub> and X<sub>6</sub> is C; R<sub>1</sub> = H, alkyl; R<sub>2</sub>, R<sub>2a</sub>, R<sub>2b</sub>, R<sub>2c</sub> = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R<sub>3</sub> = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxy carbonylamino, aryloxycarbonylamino, etc.; Y = CO<sub>2</sub>R (where R = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR<sub>4a</sub>)R<sub>5</sub> [where R<sub>4a</sub> = H, a prodrug ester; R<sub>5</sub> = alkyl, aryl, or a phosphonic acid of the structure P(O)(OR<sub>4a</sub>)<sub>2</sub>] including all stereoisomers thereof, prodrug esters thereof, and pharmaceutically acceptable salts thereof are prepared These compds. such as N-[[4-(1,2,3-triazol-4-ylmethoxy)benzyl] (4-methoxyphoxycarbonyl)amino]acetic acid N-[[4-[2-(1,2,3-triazol-4-yl)ethoxy]benzyl] (4-methoxyphoxycarbonyl)amino]acetic acid, N-[[1-[4-(2- or 4-imidazolylmethoxy)phenyl]isopentyl] (4-methoxyphoxycarbonyl)amino]acetic acid, N-[[1-[4-(1,2,4-oxadiazol-3-ylmethoxy)phenyl]isopentyl] (4-methoxyphoxycarbonyl)amino]acetic acid, N-[[4-(1,2,4-oxadiazol-3-ylmethoxy)phenethyl] (isobutoxycarbonyl)amino]acetic acid derivs. modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty acid (NEFA) and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia, hyperinsulinemia, hyperlipidemia, obesity, atherosclerosis, and related diseases.



IC ICM A61K  
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1  
IT **Stomach, disease**  
(gastric ulceritis; preparation of substituted heterocyclic  
derivs. as antidiabetic and antiobesity agents)  
IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 56-03-1,  
Biguanide 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies  
94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol  
637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid,  
derivs. 4205-91-8, Clonidine monohydrochloride 10238-21-8, Glyburide  
14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride  
21187-98-4, Glliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol  
25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol  
49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3,  
Ticlopidine 56180-94-0, Acarbose **62571-86-2**, Captopril  
72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin  
**75847-73-3**, Enalapril **76547-98-3**, Lisinopril  
79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin  
**85441-61-8**, Quinapril **86541-75-5**, Benazepril  
**87333-19-5**, Ramipril 89750-14-1, Glucagon-like peptide I  
93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat  
97240-79-4, Topiramate **98048-97-6**, Fosinopril  
**103775-10-6**, Moexipril 105816-04-4, Nateglinide 106650-56-0,  
Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate  
113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4,  
Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide  
137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993  
143443-90-7, Ifetroban 144288-97-1, TS-962 144701-48-4, Telmisartan  
147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2,  
Gemopatrilat 161600-01-7, Isaglitazone 163222-33-1, Ezetimibe  
166518-60-1, Avasimibe 168273-06-1, Rimonabant 170861-63-9, JTT-501  
176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel  
196808-45-4 199113-98-9, Balaglitazone 199914-96-0, YM-440  
213252-19-8, KRP297 244081-42-3, AJ9677 251572-86-8, P32/98  
282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9,  
R-119702 335149-15-0, KAD1129 335149-17-2, ARHO 39242 335149-19-4,  
GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648  
430433-17-3, Glipyrider 444069-80-1, Axokine  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combination therapy; preparation of substituted heterocyclic derivs. as  
antidiabetic and antiobesity agents)

L67 ANSWER 17 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:950839 HCAPLUS

DOCUMENT NUMBER: 140:696

TITLE: Combination of a DPP IV inhibitor and a cardiovascular  
compound

INVENTOR(S): Holmes, David Grenville; Shetty, Suraj Shivappa;  
Hughes, Thomas Edward

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003099279      A1      20031204      WO 2003-EP5639      20030528 <--
W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
    CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
    HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU,
    LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC,
    SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW
RW:  AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
    DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
    SI, SK, TR
CA 2487167      AA      20031204      CA 2003-2487167      20030528 <--
EP 1511484      A1      20050309      EP 2003-755149      20030528
R:   AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
    IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003011397      A      20050315      BR 2003-11397      20030528
JP 2005532330      T2      20051027      JP 2004-506803      20030528
NO 2004005557      A      20050228      NO 2004-5557      20041220
PRIORITY APPLN. INFO.:      GB 2002-12412      A 20020529
                                WO 2003-EP5639      W 20030528

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AB The invention relates to a combination therapy, such as a combined preparation or pharmaceutical composition, resp., comprising of a DPP IV inhibitor or a pharmaceutically acceptable salt thereof and a cardiovascular compound (being different from a statin) or a pharmaceutically acceptable salt thereof. The invention furthermore relates to the use of such a combination for the prevention, delay of progression or treatment of diseases and disorders selected from the group consisting of hypertension, congestive heart failure, left ventricular hypertrophy, peripheral arterial disease, diabetes, especially type 2 diabetes mellitus, diabetic retinopathy, macular degeneration, cataract, diabetic nephropathy, glomerulosclerosis, chronic renal failure, diabetic neuropathy, syndrome X, premenstrual syndrome, coronary heart disease, angina pectoris, thrombosis, atherosclerosis, myocardial infarction, transient ischemic attacks, stroke, vascular restenosis, hyperglycemia, hyperinsulinemia, hyperlipidemia, hypertrygliceridemia, insulin resistance, impaired glucose metabolism, conditions of impaired glucose tolerance, conditions of impaired fasting plasma glucose, obesity, erectile dysfunction, skin and connective tissue disorders, foot **ulcerations** and **ulcerative colitis**, endothelial dysfunction and impaired vascular compliance.

IC ICM A61K031-454

ICS A61K031-40; A61K031-16; A61P003-10; A61K031-41

CC 1-4 (Pharmacology)

Section cross-reference(s): 63

IT 9015-82-1, **Angiotensin converting** enzyme 9015-94-5,  
Renin, biological studies 54249-88-6, DPP IV 82707-54-8, Neutral  
endopeptidase 122933-89-5, Aldosterone synthase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(combination of DPP IV **inhibitor** and cardiovascular compound)

IT 58-93-5, Hydrochlorothiazide 51384-51-1, Metoprolol 74191-85-8,  
Doxazosin 75847-73-3, Enalapril 76547-98-3, Lisinopril  
86541-75-5, Benazepril 87333-19-5, Ramipril  
88150-42-9, Amlodipine 102676-47-1, Fadrozole 102676-87-9,  
(+)-Fadrozole 107724-20-9, Eplerenone 112573-73-6, Sinorphan  
114798-26-4, Losartan 123122-55-4, Candoxatril 137862-53-4, Valsartan  
144689-24-7, Olmesartan 147536-97-8, Bosentan 167305-00-2, Omapatrilat  
173334-57-1, Aliskiren 247016-69-9 274901-16-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(combination of DPP IV inhibitor and cardiovascular compound)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 18 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:845158 HCAPLUS

DOCUMENT NUMBER: 140:314987

TITLE: Pro-inflammatory Effect of Quercetin by Dual  
**Blockade of Angiotensin**  
**Converting-enzyme and Neutral Endopeptidase In**  
 Vivo

AUTHOR(S): Nicolau, M.; Dovichi, S. s.; Cuttle, G.

CORPORATE SOURCE: Dept. de Ciencias Fisiologicas, Centro di Ciencias  
 Biologicas, Univ. Federal de Santa Catarina,  
 Florianopolis, 88040-900, Brazil

SOURCE: Nutritional Neuroscience (2003), 6(5),  
 309-316

CODEN: NNINFE; ISSN: 1028-415X

PUBLISHER: Taylor &amp; Francis Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of the flavonoid quercetin on substance P- and bradykinin-induced plasma extravasation in rat tissues (duodenum, heart, pancreas, trachea and urinary bladder) was studied, and its modulation by endogenous peptidases. Plasma protein extravasation was assayed by extravasated Evans blue dye. I.v. injection of substance P (1, 3 and 10 nmol/kg) increased the plasma extravasation in a dose-dependent manner in heart, pancreas, trachea and urinary bladder. Bradykinin (3 and 10 nmol/kg, i.v.) increased plasma extravasation in a dose-dependent manner in duodenum, pancreas, trachea and urinary bladder. Pre-treatment with a selected dose of quercetin potentiated the substance P-induced plasma extravasation in heart, pancreas and urinary bladder, and also the bradykinin-induced plasma extravasation in duodenum, heart, trachea and urinary bladder. The selective pharmacol. **inhibition** of neutral endopeptidase and **angiotensin-converting enzyme** potentiated the substance P- and bradykinin-induced plasma extravasation, resp.; furthermore, treatment with receptor **antagonists** showed that the mediators involved in the potentiation of plasma extravasation by quercetin are substance P and bradykinin. Anal. of plasma **angiotensin-converting enzyme** activity demonstrated that quercetin **inhibited** this enzyme. These results suggest that quercetin potentiates plasma extravasation induced by substance P and bradykinin, and that this may result from inhibition of the degradative enzymes of these peptides.

CC 1-12 (Pharmacology)

Section cross-reference(s): 2, 18

IT Intestine

(duodenum; pro-inflammatory effect of quercetin by dual  
**blockade of angiotensin converting-enzyme**  
 and neutral endopeptidase in rat tissue)

IT Blood vessel

(permeability; pro-inflammatory effect of quercetin by dual  
**blockade of angiotensin converting-enzyme**  
 and neutral endopeptidase in rat tissue)

IT Biological transport

(permeation, vascular; pro-inflammatory effect of quercetin by dual  
**blockade of angiotensin converting-enzyme**  
 and neutral endopeptidase in rat tissue)

IT Bladder

Heart

Inflammation

Pancreas

Trachea (anatomical)

(pro-inflammatory effect of quercetin by dual **blockade** of  
**angiotensin converting**-enzyme and neutral  
 endopeptidase in rat tissue)

IT 117-39-5, Quercetin

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (pro-inflammatory effect of quercetin by dual **blockade** of  
**angiotensin converting**-enzyme and neutral  
 endopeptidase in rat tissue)

IT 58-82-2, Bradykinin 9015-82-1, **Angiotensin-converting**  
 enzyme 33507-63-0, Substance P peptide 82707-54-8, Neutral  
 endopeptidase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (pro-inflammatory effect of quercetin by dual **blockade** of  
**angiotensin converting**-enzyme and neutral  
 endopeptidase in rat tissue)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 19 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:656421 HCAPLUS

DOCUMENT NUMBER: 139:197489

TITLE: Preparation of azolecarboxylic acids useful as  
 antidiabetic and antiobesity agents

INVENTOR(S): Cheng, Peter T.; Zhang, Hao; Hariharan, Narayanan

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 81 pp., Cont.-in-part of U.S.  
 Ser. No. 153,454.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

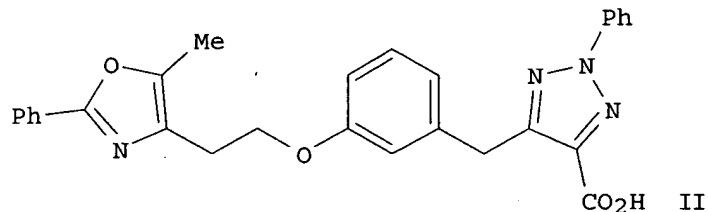
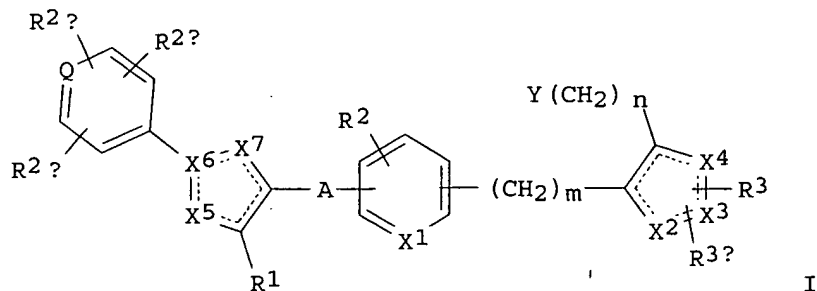
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003158232	A1	20030821	US 2002-294525	20021114 <--
US 6967212	B2	20051122		
US 2003092736	A1	20030515	US 2002-153454	20020522 <--
US 2005124661	A1	20050609	US 2004-12810	20041215
PRIORITY APPLN. INFO.:			US 2001-294380P	P 20010530
			US 2002-153454	A2 20020522
			US 2002-294525	A3 20021114

OTHER SOURCE(S): MARPAT 139:197489

GI



AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH<sub>2</sub>)<sub>x</sub>, (CH<sub>2</sub>)<sub>x1</sub>, (CH<sub>2</sub>)<sub>x20</sub>(CH<sub>2</sub>)<sub>x3</sub>; x = 1-5; x<sub>1</sub> = 2-5; x<sub>2</sub>, x<sub>3</sub> = 0-5; ≥1 of x<sub>2</sub>, x<sub>3</sub> ≠ 0; X<sub>1</sub> = CH, N; X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub>, X<sub>5</sub>, X<sub>7</sub> = C, N, O, S; in each of X<sub>1</sub>-X<sub>7</sub>, C may include CH; R<sub>1</sub> = H, alkyl; R<sub>2</sub> = H, alkyl, alkoxy, halo, (substituted) amino; R<sub>2a</sub>, R<sub>2b</sub> and R<sub>2c</sub> = H, alkyl, alkoxy, halo, (substituted) amino; R<sub>3</sub>, R<sub>3a</sub> = H, alkyl, arylalkyl, aryloxycarbonyl, alkylloxycarbonyl, alkynylloxycarbonyl, alkenylloxycarbonyl, arylcarbonyl, etc.; Y = CO<sub>2</sub>R<sub>4</sub>, 1-tetrazolyl, P(O)(OR<sub>4a</sub>)R<sub>5</sub>, P(O)(OR<sub>4a</sub>)<sub>2</sub>; R<sub>4</sub> = H, alkyl, prodrug ester; R<sub>4a</sub> = H, prodrug ester; R<sub>5</sub> = alkyl, aryl; with provisos], were prepared as simultaneous inhibitors of peroxisome proliferator activated receptor-γ (PPAR<sub>γ</sub>) and stimulators of peroxisome proliferator activated receptor-α (PPAR<sub>α</sub>). Thus, title compound (II) (prepared starting from Meldrum's acid 3-methoxyphenylacetyl chloride) bound to human PPAR<sub>α</sub> and to PPAR<sub>γ</sub> ligand binding domains with IC<sub>50</sub> = 69 nM.

IC ICM A61K031-444

ICS A61K031-4439; A61K031-427; A61K031-422; C07D417-02; C07D417-14; C07D413-14; C07D413-02

INCL 514333000; 514340000; 514341000; 514342000; 514367000; 514375000; 514397000; 546256000; 546269700; 546271400

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63

IT **Stomach, disease**

(ulcer, treatment; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

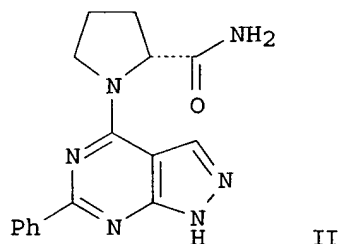
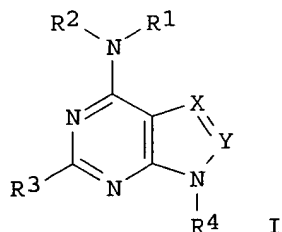
IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 58-32-2, Dipyrindamole 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 4205-91-8, Clonidine hydrochloride 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Glucilazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 55142-85-3, Ticlopidine 56180-94-0, Acarbose 62571-86-2, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril

76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8,  
 Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril  
 86541-75-5, Benazepril 87333-19-5, Ramipril  
 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat  
 97240-79-4, Topiramate 98048-97-6, Fosinopril  
 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0,  
 Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate  
 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4,  
 Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide  
 137862-53-4, Valsartan 138402-11-6, Irbesartan 143443-90-7, Ifetroban  
 144288-97-1, Ts-962 145599-86-6, Cerivastatin 152755-31-2, Ly295427  
 159183-92-3, 1750355 160135-92-2, Gemopatrilat 161600-01-7,  
 Isaglitazone 166518-60-1, Avasimibe 167305-00-2, Omapatrilat  
 169319-62-4, Cgs 30440 170861-63-9, Jtt-501 178759-95-0, MD 700  
 182815-44-7, Cholestagel 196808-45-4 199113-98-9 199914-96-0, Ym-440  
 213252-19-8, Krp297 244081-42-3, Aj9677 251572-86-8, p32/98  
 282526-98-1, Atl-962 287714-41-4, Visastatin 335149-08-1, 1895645  
 335149-14-9, r-119702 335149-15-0, Kad1129 335149-17-2, Arho39242  
 335149-19-4, Gw-409544 335149-23-0, Nvp-dpp-728a 335149-25-2, Cp331648  
 430433-17-3, Glipyride 444069-80-1, Axokine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (coadministration; preparation of azolecarboxylic acids useful as  
 antidiabetic and antiobesity agents)

L67 ANSWER 20 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:570644 HCAPLUS  
 DOCUMENT NUMBER: 139:133575  
 TITLE: Preparation of bicyclic pyrimidinyl derivatives as  
 adenosine receptor ligands  
 INVENTOR(S): Castelhana, Arlindo L.; McKibben, Bryan  
 PATENT ASSIGNEE(S): OSI Pharmaceuticals Inc., USA  
 SOURCE: U.S. Pat. Appl. Publ., 105 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003139427	A1	20030724	US 2002-227378	20020823 <--
PRIORITY APPLN. INFO.:			US 2002-227378	20020823
OTHER SOURCE(S):	MARPAT 139:133575			
GI				



AB Title compds. I [Y = N, CR5 and X = N, CR6 wherein X, Y are both N or when Y = CR5, X = N or when X = CR6, Y = N; R1-2 = H, alkoxy, aminoalkyl, etc; R3-4 = H, alkyl, aryl, alkylaryl] are prepared For instance, 3-amino-4-carbamoylpyrazole is acylated with benzoyl chloride (Pyridine, 50°, 5-6 h), cyclized to the corresponding pyrazolopyrimidine (water, K<sub>2</sub>CO<sub>3</sub>, 100°, 16 h), converted to the chloride (POCl<sub>3</sub>, 106°, 2 h) and used for reactions with various amines to give the example compds., e.g., II. II has K<sub>i</sub> = 76.7 nM for the adenosine A<sub>1</sub> receptor, K<sub>i</sub> = 242.7 nM for A<sub>2a</sub> and K<sub>i</sub> = 1480.5 nM for A<sub>2b</sub>. I are useful for the treatment of.

IC ICM C07D487-02  
ICS A61K031-52; A61K031-519

INCL 514261100; 514262100; 514263200; 514263400; 544277000; 544262000; 544254000

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1

IT **Intestine, disease**  
(**inflammatory**; preparation of bicyclic pyrazolo- imidazo- and triazolopyrimidinyl derivs. as adenosine receptor ligands)

IT **Inflammation**  
**Intestine, disease**  
(**ulcerative colitis**; preparation of bicyclic pyrazolo- imidazo- and triazolopyrimidinyl derivs. as adenosine receptor ligands)

IT 9015-82-1, **Angiotensin-converting enzyme**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**inhibitors**, combination pharmaceutical; preparation of bicyclic pyrazolo- imidazo- and triazolopyrimidinyl derivs. as adenosine receptor ligands)

L67 ANSWER 21 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:132967 HCAPLUS  
DOCUMENT NUMBER: 138:163546  
TITLE: Methods and compositions for treating diseases associated with excesses in ACE  
INVENTOR(S): Moskowitz, David W.  
PATENT ASSIGNEE(S): Genomed, LLC, USA  
SOURCE: PCT Int. Appl., 44 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013434	A2	20030220	WO 2002-US25001	20020806 <--
WO 2003013434	A3	20030828		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

JP 2005503378 T2 20050203 JP 2003-518448 20020806  
 PRIORITY APPLN. INFO.: US 2001-310064P P 20010806  
 US 2002-347013P P 20020111  
 US 2002-347905P P 20020115  
 US 2002-350563P P 20020124  
 US 2002-352072P P 20020128  
 US 2002-352074P P 20020128  
 US 2002-352484P P 20020130  
 US 2002-378467P P 20020508  
 US 2002-379796P P 20020513  
 US 2002-380741P P 20020516  
 WO 2002-US25001 W 20020806

AB Over 40 common diseases, in addition to congestive heart failure (CHF) due to hypertension (HTN) or non-insulin dependent diabetes mellitus (type II diabetes mellitus) (NIDDM), atherosclerotic peripheral vascular disease (ASPVD) due to HTN or NIDDM, and chronic obstructive pulmonary disease; emphysema (COPD), are associated with the ACE D/D genotype and should also respond to an adequate tissue-ID of **ACE inhibitors** such as quinapril. Several of these diseases have now been successfully treated using higher than normal dosages of **ACE inhibitors**, especially hydrophobic **ACE inhibitors**, with good outcomes. **ACE inhibitors** have also been found to be useful in inhibiting apoptosis and aging in general. Dosages that have been utilized are typically greater than quinapril at a dose of 40 to 80 mg/day, i.e. up to 1 mg/kg per day for a "typical" 80 kg patient. New formulations of **ACE inhibitors** have been developed for these higher dosages, including 80 mg tablets, controlled and/or sustained release formulations, and formulations containing a second active agent such as a diuretic, or a compound such as furosemide 20 mg/day (for creatinine <2.5 mg/dL) or furosemide 40 mg/day (for creatinine >2.5 mg/dL), to prevent fluid retention and congestive heart failure in patients with renal failure. The **ACE inhibitors** can also be combined with an angiotensin receptor blocker.

IC ICM A61K

CC 1-8 (Pharmacology)

Section cross-reference(s): 7, 63

ST disease assocd excess angiotensin converting enzyme treatment; **ACE inhibitor** dosage disease treatment; formulation **ACE inhibitor**

IT Hepatitis

(A, treatment of; **ACE inhibitor** dosages and

formulations for treating diseases associated with excesses in ACE)

IT Feed

(**ACE inhibitor** administration in; **ACE**

**inhibitor** dosages and formulations for treating diseases

associated with excesses in ACE)

IT Allergy inhibitors

Anti-AIDS agents

Anti-Alzheimer's agents

Antiasthmatics

Antidepressants

Antiglaucoma agents

Antihypertensives

Antiobesity agents

Antiparkinsonian agents

Antirheumatic agents

Antitumor agents

Antiulcer agents

Anxiolytics



Drug delivery systems  
Human  
Human groups  
Tuberculostatics  
    (ACE inhibitor dosages and formulations for  
    treating diseases associated with excesses in ACE)

IT Blood serum  
    (ACE inhibitor in combination with fludrocortisone  
    acetate in relation to potassium ion concentration in; ACE  
    inhibitor dosages and formulations for treating diseases  
    associated with excesses in ACE)

IT Angiotensin receptor antagonists  
Diuretics  
    (ACE inhibitor in combination with; ACE  
    inhibitor dosages and formulations for treating diseases  
    associated with excesses in ACE)

IT Hepatitis  
    (B, treatment of; ACE inhibitor dosages and  
    formulations for treating diseases associated with excesses in ACE)

IT Genotypes  
    (D/D of ACE DCP1 gene, diseases in relation to; ACE  
    inhibitor dosages and formulations for treating diseases  
    associated with excesses in ACE)

IT Gene, animal  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
    (DCP1, for ACE, D/D genotype, diseases in relation to; ACE  
    inhibitor dosages and formulations for treating diseases  
    associated with excesses in ACE)

IT Kidney, disease  
    (HIV-associated, treatment of; ACE inhibitor dosages  
    and formulations for treating diseases associated with excesses in ACE)

IT Kidney, disease  
    (IgA nephropathy, treatment of; ACE inhibitor  
    dosages and formulations for treating diseases associated with excesses in  
    ACE)

IT Bone, disease  
    (Paget's, treatment of; ACE inhibitor dosages and  
    formulations for treating diseases associated with excesses in ACE)

IT Drugs of abuse  
    (abuse of, treatment of; ACE inhibitor dosages and  
    formulations for treating diseases associated with excesses in ACE)

IT Tobacco smoke  
    (abuse, treatment of; ACE inhibitor dosages and  
    formulations for treating diseases associated with excesses in ACE)

IT Blood vessel  
    (access in end-stage renal disease; ACE inhibitor  
    dosages and formulations for treating diseases associated with excesses in  
    ACE)

IT Inflammation  
Reproductive system, disease  
    (adnexitis, treatment of; ACE inhibitor dosages and  
    formulations for treating diseases associated with excesses in ACE)

IT Hepatitis  
    (alc., treatment of; ACE inhibitor dosages and  
    formulations for treating diseases associated with excesses in ACE)

IT Allergy  
Inflammation  
Nose, disease  
    (allergic rhinitis, treatment of; ACE inhibitor

- dosages and formulations for treating diseases associated with excesses in ACE)
- IT Angiotensin receptor antagonists  
(angiotensin II, **ACE inhibitor** in combination with;  
**ACE inhibitor** dosages and formulations for treating  
diseases associated with excesses in ACE)
- IT Antiarteriosclerotics  
(antiatherosclerotics; **ACE inhibitor** dosages and  
formulations for treating diseases associated with excesses in ACE)
- IT Disease, animal  
(associated with excess ACE, treatment of; **ACE inhibitor**  
dosages and formulations for treating diseases associated with excesses in  
ACE)
- IT Skin, neoplasm  
(basal cell carcinoma, treatment of; **ACE inhibitor**  
dosages and formulations for treating diseases associated with excesses in  
ACE)
- IT Carcinoma  
(basal cell, treatment of; **ACE inhibitor** dosages  
and formulations for treating diseases associated with excesses in ACE)
- IT Mental and behavioral disorders  
(bipolar disorder; **ACE inhibitor** dosages and  
formulations for treating diseases associated with excesses in ACE)
- IT Gallbladder, disease  
Inflammation  
(cholecystitis, treatment of; **ACE inhibitor** dosages  
and formulations for treating diseases associated with excesses in ACE)
- IT Lung, disease  
(chronic obstructive, treatment of; **ACE inhibitor**  
dosages and formulations for treating diseases associated with excesses in  
ACE)
- IT Drug delivery systems  
(controlled-release; **ACE inhibitor** dosages and  
formulations for treating diseases associated with excesses in ACE)
- IT Kidney, disease  
(cyst, acquired renal cystic disease of end-stage renal disease,  
treatment of; **ACE inhibitor** dosages and  
formulations for treating diseases associated with excesses in ACE)
- IT Mental and behavioral disorders  
(dementia, multi-infarct, treatment of; **ACE inhibitor**  
dosages and formulations for treating diseases associated with excesses in  
ACE)
- IT Mental and behavioral disorders  
(dementia, treatment of; **ACE inhibitor** dosages and  
formulations for treating diseases associated with excesses in ACE)
- IT Mental and behavioral disorders  
(depression, treatment of; **ACE inhibitor** dosages  
and formulations for treating diseases associated with excesses in ACE)
- IT Nerve, disease  
(diabetic neuropathy, treatment of; **ACE inhibitor**  
dosages and formulations for treating diseases associated with excesses in  
ACE)
- IT Eye, disease  
(diabetic retinopathy, treatment of; **ACE inhibitor**  
dosages and formulations for treating diseases associated with excesses in  
ACE)
- IT Joint, anatomical  
(disease, degeneration, treatment of; **ACE inhibitor**  
dosages and formulations for treating diseases associated with excesses in

- ACE)
- IT Inflammation  
Intestine, disease  
(diverticulitis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Intestine, disease  
(diverticulosis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Lung, disease  
(embolism, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Hypertension  
(end-stage renal disease with, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Kidney, disease  
(failure, chronic, irreversible, with hypertension or type II diabetes, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Kidney, disease  
(failure, due to hypertension or type II diabetes, delay progression of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Inflammation  
Kidney, disease  
(focal segmental glomerulonephritis, end-stage renal disease due to, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Hip  
(fractures, prevention of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Inflammation  
Stomach, disease  
(gastritis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Digestive tract, disease  
(gastroesophageal reflux, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Infection  
(hepatitis A, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Infection  
(hepatitis B, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Musculoskeletal diseases  
(hernia, hiatal or inguinal hernia, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Lipids, biological studies  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(hyperlipidemia, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Intestine, disease  
(inflammatory, treatment of; **ACE inhibitor**

- dosages and formulations for treating diseases associated with excesses in ACE)
- IT Animal tissue  
(inhibition of ACE of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Apoptosis  
(inhibition of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Intestine, disease  
(irritable bowel syndrome, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Brain, disease  
(ischemia, transient, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Disease, animal  
(joint degeneration, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Heart, disease  
(left ventricle, hypertrophy, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Hypertrophy  
(left ventricular, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Inflammation  
Kidney, disease  
(membranous glomerulonephritis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Inflammation  
Kidney, disease  
(mesangial proliferative glomerulonephritis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Headache  
(migraine, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Diabetes mellitus  
(non-insulin-dependent, end-stage renal disease with, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Kidney, disease  
(obstructive uropathy, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Hydrophobicity  
(of **ACE inhibitor**; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Inflammation  
Pancreas, disease  
(pancreatitis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Ulcer  
(peptic, treatment of; **ACE inhibitor** dosages and

- formulations for treating diseases associated with excesses in ACE)
- IT Blood vessel, disease  
(peripheral, atherosclerotic, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Hearing loss  
(presbycusis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Aging, animal  
(progressive loss of hearing in, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Embolism  
Hypertension  
(pulmonary, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Cyst, pathological  
(renal, acquired renal cystic disease of end-stage renal disease, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Inflammation  
Nose, disease  
(rhinitis, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Connective tissue, disease  
(scleroderma, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Inflammation  
Respiratory system, disease  
(sinusitis, allergic, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Neoplasm  
(solid, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Brain, disease  
(stroke, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Drug delivery systems  
(sustained-release; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Lupus erythematosus  
(systemic, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Drug delivery systems  
(tablets, chewable; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Drug delivery systems  
(tablets; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Hyperparathyroidism  
(tertiary, in end-stage renal disease, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Drug allergy  
(to penicillin or sulfa, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Ischemia

- (transient cerebral, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Human immunodeficiency virus  
(treatment of infection with or complications of infection with; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Animal  
(treatment of non-human; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT AIDS (disease)  
Allergy  
Alzheimer's disease  
Anxiety  
Ascites  
Asthma  
Atherosclerosis  
Calculi, biliary  
Calculi, renal  
Cataract  
Cirrhosis  
Eczema  
Emphysema  
Glaucoma (disease)  
Gout  
Headache  
Hypercholesterolemia  
Hypertriglyceridemia  
Hypothyroidism  
Leukemia  
Lymphoma  
Obesity  
Osteoarthritis  
Osteoporosis  
Parkinson's disease  
Psoriasis  
Rheumatoid arthritis  
Schizophrenia  
Seizures  
Tuberculosis  
(treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Digestive tract, disease  
(ulcer, peptic, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT Thrombosis  
(venous, treatment of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT 514-36-3, Fludrocortisone acetate  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**ACE inhibitor** administration in combination with; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT 62571-86-2, Captopril 75847-73-3, Enalapril  
76547-98-3, Lisinopril 85441-61-8, Quinapril  
86541-75-5, Benazepril 87333-19-5, Ramipril  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (**ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT 52-39-1, Aldosterone  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(administration with **ACE inhibitor**; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT 9015-82-1, **Angiotensin-converting** enzyme  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(**inhibitors**; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT 24203-36-9, Potassium ion, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(of serum, **ACE inhibitor** in combination with fludrocortisone acetate in relation to; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT 127-31-1, Florinef  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(quinapril with; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT 1406-05-9, Penicillin  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(treatment of allergy to; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)
- IT 57-88-5, Cholesterol, biological studies  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(treatment of high levels of; **ACE inhibitor** dosages and formulations for treating diseases associated with excesses in ACE)

L67 ANSWER 22 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:80434 HCAPLUS  
DOCUMENT NUMBER: 138:180722  
TITLE: Method for the treatment of gastric ulcer disease in patients with decreased gastric secretion  
INVENTOR(S): Medvedev, V. N.; Ivkova, I. A.  
PATENT ASSIGNEE(S): Ivanovskaya Gosudarstvennaya Meditsinskaya Akademiya, Russia  
SOURCE: Russ., No pp. given  
CODEN: RUXXE7  
DOCUMENT TYPE: Patent  
LANGUAGE: Russian  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2188010	C2	20020827	RU 2000-110867	20000427 <--
PRIORITY APPLN. INFO.:			RU 2000-110867	20000427

AB Method is disclosed for the treatment of gastric ulcer disease in patients with decreased gastric acid secretion. Method involves treatment with ranitidine at half of a dose of 75 mg/d together with captopril (**capoten**) at the dose of 12.5 mg twice daily for a month. Method provides a purposeful action upon the processes of ulcer reparation. Method ensures higher efficiency of treatment.

IC ICM A61K031-341  
ICS A61K031-401; A61P001-04  
CC 1-9 (Pharmacology)  
ST ranitidine captopril antiulcer human gastric ulcer disease;  
**capoten** ranitidine gastric acid hyposecretion **stomach**  
**ulcer** disease human  
IT **Stomach**  
(antrum, gastric **ulcer** localized in; method for treatment of  
gastric ulcer disease in patients with decreased gastric secretion)  
IT Inflammation  
**Stomach, disease**  
(atrophic gastritis; method for treatment of gastric **ulcer**  
disease in patients with decreased gastric secretion)  
IT **Stomach**  
(fundus, gastric **ulcer** localized in; method for treatment of  
gastric ulcer disease in patients with decreased gastric secretion)  
IT **Stomach**  
(pylorus, gastric **ulcer** localized in; method for treatment of  
gastric ulcer disease in patients with decreased gastric secretion)  
IT **Stomach, disease**  
(**ulcer**; method for treatment of gastric **ulcer**  
disease in patients with decreased gastric secretion)  
IT 62571-86-2, Captopril 66357-35-5, Ranitidine  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(method for treatment of gastric ulcer disease in patients with  
decreased gastric secretion)

L67 ANSWER 23 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:978628 HCAPLUS  
DOCUMENT NUMBER: 138:49938  
TITLE: Nucleic acids for the prevention and treatment of  
gastric ulcers  
INVENTOR(S): Bratzler, Robert L.; Petersen, Deanna M.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 45 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002198165	A1	20021226	US 2001-920313	20010801 <--
PRIORITY APPLN. INFO.:			US 2000-222248P	P 20000801

OTHER SOURCE(S): MARPAT 138:49938

AB The invention relates to methods and products for treating gastric ulcers.  
A nucleic acid and optionally an anti-ulcer agent are administered to a  
subject to prevent or treat gastric ulcer.

IC ICM A61K048-00

INCL 514044000

CC 1-9 (Pharmacology)

IT **Stomach, disease**

(**ulcer**; nucleic acids for prevention and treatment of gastric  
ulcers in relation to immunostimulation and combination with other  
agents)

IT 35115-60-7, Teprotide 62571-86-2, Captopril 63250-36-2,  
Epicaptopril 74258-86-9, Alacepril 75107-57-2 75176-37-3,



Zofenoprilat 75479-46-8 75847-73-3, Enalapril 76095-16-4, Enapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 78636-30-3 80828-34-8, Indolaprilat 80876-01-3, Indolapril 80943-05-1, Converstatin 81045-50-3, Pivalopril 81872-10-8, Zofenopril 82586-55-8, Quinapril hydrochloride 82768-85-2, Quinaprilat 82834-16-0, Perindopril 82924-03-6, Pentopril 83059-56-7, Zabicipril 83398-08-7 83435-66-9, Delapril 83602-05-5, Spiraprilat 83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril 85921-53-5, Altiopril calcium 86541-74-4, Benazepril hydrochloride 86541-75-5, Benazepril 86541-78-8, Benazeprilat 87269-97-4, Ramiprilat 87333-19-5, Ramipril 87679-37-6, Trandolapril 87679-71-8, Trandolaprilat 88201-41-6, Ancovenin 88768-40-5, Cilazapril 88889-14-9 89371-37-9, Imidapril 90103-92-7, Zabiciprilat 90139-06-3, Cilazaprilat 90965-60-9, Muracein A 90965-61-0, Muracein B 91105-26-9, Muracein C 94841-17-5, Spirapril hydrochloride 95153-31-4, Perindoprilat 95399-71-6, Fosfenopril 98048-97-6, Fosenopril 100157-28-6, Foroxymithine 103775-10-6, Moexipril 103775-14-0, Moexiprilat 103930-64-9, Hemorphin-4 109214-55-3, Libenzapril 109683-61-6, Utibapril 110221-44-8, Temocapril hydrochloride 111223-26-8, Ceranapril 111902-57-9, Temocapril 113082-98-7, Enalkiren 125708-06-7, Lyciumin A 125756-66-3, Lyciumin B 127420-24-0, Idrapril 135038-56-1, Glycopril 135038-57-2, Alatriopril 156039-69-9, Mixanpril

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ACE inhibitor; nucleic acids for prevention and treatment of gastric ulcers in relation to immunostimulation and combination with other agents)

IT 9015-82-1, **Angiotensin-converting** enzyme

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; nucleic acids for prevention and treatment of gastric ulcers in relation to immunostimulation and combination with other agents)

L67 ANSWER 24 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:927185 HCAPLUS

DOCUMENT NUMBER: 138:24716

TITLE: Preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents

INVENTOR(S): Cheng, Peter T.; Zhang, Hao; Hariharan, Narayanan

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 169 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096358	A2	20021205	WO 2002-US16633	20020523 <--
WO 2002096358	A3	20030327		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2449160 AA 20021205 CA 2002-2449160 20020523 <--

EP 1390363 A2 20040225 EP 2002-729306 20020523 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

TR 200400650 T3 20040621 TR 2004-200400650 20020523 <--

JP 2004536070 T2 20041202 JP 2002-592871 20020523 <--

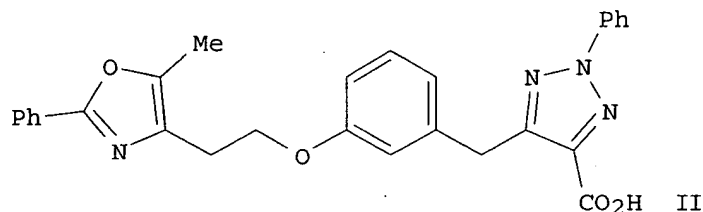
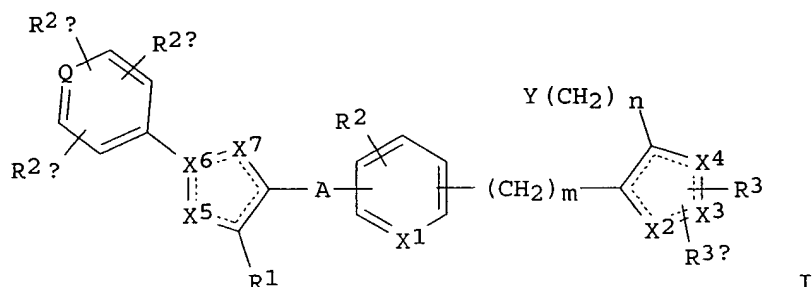
PRIORITY APPLN. INFO.:

US 2001-294380P P 20010530

WO 2002-US16633 W 20020523

OTHER SOURCE(S): MARPAT 138:24716

GI



AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH<sub>2</sub>)<sub>x</sub>, (CH<sub>2</sub>)<sub>x1</sub>, (CH<sub>2</sub>)<sub>x20</sub>(CH<sub>2</sub>)<sub>x3</sub>; x = 1-5; x<sub>1</sub> = 2-5; x<sub>2</sub>, x<sub>3</sub> = 0-5; ≥1 of x<sub>2</sub>, x<sub>3</sub> ≠ 0; X<sub>1</sub> = CH, N; X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub>, X<sub>5</sub>, X<sub>7</sub> = C, N, O, S; in each of X<sub>1</sub>-X<sub>7</sub>, C may include CH; R<sub>1</sub> = H, alkyl; R<sub>2</sub> = H, alkyl, alkoxy, halo, (substituted) amino; R<sub>2a</sub>, R<sub>2b</sub> and R<sub>2c</sub> = H, alkyl, alkoxy, halo, (substituted) amino; R<sub>3</sub>, R<sub>3a</sub> = H, alkyl, arylalkyl, aryloxy carbonyl, alkyl oxy carbonyl, alkynyl oxy carbonyl, alkenyl oxy carbonyl, aryl carbonyl, alkyl carbonyl, aryl, heteroaryl, alkyl(halo) aryloxy carbonyl, alkoxy(halo) aryloxy carbonyl, cycloalkyl aryloxy carbonyl, cycloalkyl oxy aryloxy carbonyl, cycloheteroalkyl, heteroaryl carbonyl, heteroaryl heteroaryl alkyl, alkyl carbonyl amino, aryl carbonyl amino, heteroaryl carbonyl amino, alkoxy carbonyl amino, aryloxy carbonyl amino, heteroaryl heteroaryl carbonyl, alkyl sulfonyl, alkenyl sulfonyl, heteroaryl oxy carbonyl, cycloheteroalkyl oxy carbonyl, heteroaryl alkyl, aminocarbonyl, substituted aminocarbonyl, alkyl aminocarbonyl, aryl aminocarbonyl, aryloxy aryl alkyl, alkynyl oxy carbonyl, haloalkoxy aryloxy carbonyl, alkoxy carbonyl aryloxy carbonyl, aryloxy aryloxy carbonyl, aryl sulfinyl aryl carbonyl, etc.; Y = CO<sub>2</sub>R<sub>4</sub>,

1-tetrazolyl, P(O) (OR4a)R5, P(O) (OR4a)2; R4 = H, alkyl, prodrug ester; R4a = H, prodrug ester; R5 = alkyl, aryl; with provisos], were prepared as simultaneous inhibitors of peroxisome proliferator activated receptor- $\gamma$  (PPAR $\gamma$ ) and stimulators of peroxisome proliferator activated receptor- $\alpha$  (PPAR $\alpha$ ). Thus, title compound (II) (prepared starting from Meldrum's acid 3-methoxyphenylacetyl chloride) bound to human PPAR $\alpha$  and to PPAR $\gamma$  ligand binding domains with IC50 = 69 nM.

IC ICM A61K

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

IT Stomach, disease

(ulcer, treatment; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 4205-91-8, Clonidine hydrochloride 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 55142-85-3, Ticlopidine 56180-94-0, Acarbose 62571-86-2, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 98048-97-6, Fosinopril 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 143443-90-7, Ifetroban 144288-97-1, Ts-962 145599-86-6, Cerivastatin 152755-31-2, Ly295427 159183-92-3, 1750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, Cgs 30440 170861-63-9, Jtt-501 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4 199113-98-9, Nn-2344 199914-96-0, Ym-440 213252-19-8, Krp297 244081-42-3, Aj9677 251572-86-8, p32/98 282526-98-1, Atl-962 287714-41-4 335149-08-1, 1895645 335149-14-9, r-119702 335149-15-0, Kad1129 335149-17-2, Arho39242 335149-19-4, Gw-409544 335149-23-0, Nvp-dpp-728a 335149-25-2, Cp331648 430433-17-3, Glipyride 444069-80-1, Axokine RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

L67 ANSWER 25 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:927184 HCAPLUS

DOCUMENT NUMBER: 138:14048

TITLE: Preparation of oxazolyethoxyphenylprolines and related compounds as antidiabetic and antiobesity agents.

INVENTOR(S): Cheng, Peter T.; Jeon, Yoon; Wang, Wei

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

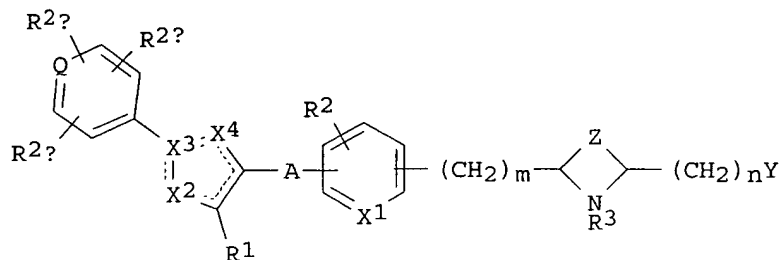
SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2

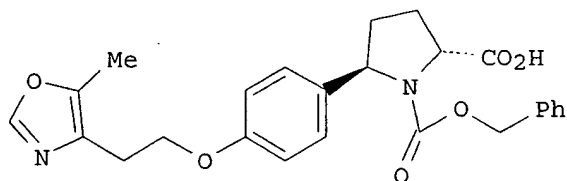
DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096357	A2	20021205	WO 2002-US16628	20020523 <--
WO 2002096357	A3	20030925		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003092697	A1	20030515	US 2002-153342	20020522 <--
CA 2449006	AA	20021205	CA 2002-2449006	20020523 <--
EP 1401433	A2	20040331	EP 2002-737192	20020523 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005506954	T2	20050310	JP 2002-592870	20020523
PRIORITY APPLN. INFO.:			US 2001-294505P	P 20010530
			WO 2002-US16628	W 20020523

OTHER SOURCE(S): MARPAT 138:14048  
 GI



I



II

AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH<sub>2</sub>)<sub>x</sub>, (CH<sub>2</sub>)<sub>x1</sub>, with an alkenyl or alkynyl bond in the chain, (CH<sub>2</sub>)<sub>x2</sub>O(CH<sub>2</sub>)<sub>x3</sub>; x = 1-5; x<sub>1</sub> = 2-5; x<sub>2</sub>, x<sub>3</sub> = 0-5; provided that ≥1 of x<sub>2</sub> and x<sub>3</sub> ≠ 0; X<sub>1</sub> = CH, N; X<sub>2</sub> = C, N, O, S; X<sub>3</sub> = C, N; X<sub>4</sub> = C, N, O, S provided that ≥1 of X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub> = N; in each of X<sub>1</sub>-X<sub>4</sub>, C may include CH; R<sub>1</sub> = H, alkyl; R<sub>2</sub> = H, alkyl, alkoxy, halo, (substituted) amino; R<sub>2a</sub>, R<sub>2b</sub> R<sub>2c</sub> = H, alkyl, alkoxy, halo, (substituted) amino; R<sub>3</sub> = H, alkyl, arylalkyl, aryloxycarbonyl, alkylloxycarbonyl, alkynylloxycarbonyl, alkenylloxycarbonyl, arylcarbonyl,

alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxy carbonylamino, heteroaryloxy carbonylamino, heteroarylheteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxy carbonyl, cycloheteroalkyloxy carbonyl, aryloxyheteroarylalkyl, heteroarylalkyloxyarylalkyl, arylarylalkyl, arylalkenylarylalkyl, arylaminoarylalkyl, etc.; Y = CO<sub>2</sub>R<sub>4</sub>, 1-tetrazolyl, P(O)(OR<sub>4a</sub>)R<sub>5</sub>, P(O)(OR<sub>4a</sub>)<sub>2</sub>; R<sub>4</sub> = H, alkyl, prodrug ester; R<sub>4a</sub> = H, prodrug ester; R<sub>5</sub> = alkyl, aryl; Z = (CH<sub>2</sub>)<sub>x4</sub>, (CH<sub>2</sub>)<sub>x5</sub>, (CH<sub>2</sub>)<sub>x6</sub>(CH<sub>2</sub>)<sub>x7</sub>; x<sub>4</sub> = 1-5; x<sub>5</sub> = 2-5; x<sub>6</sub>, x<sub>7</sub> = 0-4], were prepared as antidiabetic and antiobesity agents (no data). Thus, title compound (II) was prepared in 6 steps.

IC ICM A61K

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 34

IT Stomach, disease

(ulcer, treatment; preparation of oxazolyethoxyphenylprolines and related compds. as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 4205-91-8, Clonidine hydrochloride 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 56180-94-0, Acarbose 62571-86-2, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 98048-97-6, Fosinopril 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993 143443-90-7, Ifetroban 144288-97-1, TS-962 145599-86-6, Cerivastatin 147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, CGS 30440 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4, GI 262570 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 251565-85-2, AR-H 039242 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyrider 444069-80-1, Axokine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(coadministration; preparation of oxazolyethoxyphenylprolines and related compds. as antidiabetic and antiobesity agents)

L67 ANSWER 26 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:540258 HCAPLUS

DOCUMENT NUMBER: 137:109267

TITLE: Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors

INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S.  
 Ser. No. 875,155.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002094977	A1	20020718	US 2001-7407	20011204 <--
US 6627636	B2	20030930		
US 2002013334	A1	20020131	US 2001-875155	20010606 <--
PRIORITY APPLN. INFO.:			US 2000-211595P	P 20000615
			US 2001-875155	A2 20010606

OTHER SOURCE(S): MARPAT 137:109267  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [X = O, S, SO, SO<sub>2</sub>, NR<sub>7</sub>; Z = HOCHCH<sub>2</sub>CH(OH)CH<sub>2</sub>CO<sub>2</sub>R<sub>3</sub>, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R<sub>1</sub>, R<sub>2</sub> = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R<sub>3</sub> = H, alkyl, metal ion; R<sub>4</sub> = H, halo, CF<sub>3</sub>, etc.; R<sub>7</sub> = H, alkyl, aryl, alkanoyl, aroyl, alkoxy carbonyl, etc.; R<sub>9</sub>, R<sub>10</sub> = H, alkyl], were prepared as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). A multistep synthesis of II is reported.

IC ICM C07D498-02  
 ICS A61K031-55; A61K031-4745

INCL 514215000

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1

IT **Stomach, disease**  
 (ulcer, treatment; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-01-7, Spironolactone  
 52-53-9, Verapamil 54-31-9, Furosemide 58-32-2, Dipyridamole  
 58-93-5, Hydrochlorothiazide 59-67-6, Niacin, biological studies  
 94-20-2, Chlorpropamide 122-09-8, Phentermine 525-66-6, Propranolol  
 564-25-0, Doxycycline 637-07-0, Clofibrate 657-24-9, Metformin  
 1684-40-8, Tacrine hydrochloride 3416-24-8, Glucosamine 4205-91-8,  
 Clonidine hydrochloride 9004-61-9, Hyaluronic acid 9007-28-7,  
 Chondroitin sulfate 10118-90-8, Minocycline 10238-21-8, Glyburide  
 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride  
 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol  
 25812-30-0, Gemfibrozil 26807-65-8, Indapamide 29094-61-9, Glipizide  
 29122-68-7, Atenolol 42200-33-9, Nadolol 49562-28-9, Fenofibrate  
 55142-85-3, Ticlopidine 56180-94-0, Acarbose 56211-40-6, Torasemide  
 62571-86-2, Captopril 68475-42-3, Anagrelide 72432-03-2,

Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 98048-97-6, Fosinopril 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 113665-84-2, Clopidogrel 114798-26-4, Losartan 120014-06-4, Donepezil 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC2993 143443-90-7, Ifetroban 143653-53-6, Abciximab 144288-97-1, TS 962 144494-65-5, Tirofiban 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 152755-31-2, LY295427 159183-92-3, 1750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 162011-90-7, Vioxx 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 169319-62-4, CGS 30440 169590-42-5, Celebrex 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 188627-80-7, Eptifibatide 196808-45-4, GI-262570 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 246852-12-0, Amlodipine mesylate 251572-86-8, P32/98 282526-98-1, ATL-962 287714-41-4, Rosuvastatin 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, AR-HO39242 335149-19-4, GW-409544 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyrider 430433-43-5, CP644673 444069-80-1, Axokine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(coadministered agents; preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

L67 ANSWER 27 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:157564 HCAPLUS

DOCUMENT NUMBER: 136:205424

TITLE: Combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors

INVENTOR(S): Allison, Malcolm; Gatlin, Marjorie Regan

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Novartis Pharma GmbH

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015892	A2	20020228	WO 2001-EP9586	20010820 <--
WO 2002015892	A3	20030904		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,  
KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,  
IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002014952 A5 20020304 AU 2002-14952 20010820 <--

EP 1359907 A2 20031112 EP 2001-983442 20010820 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004519424 T2 20040702 JP 2002-520813 20010820 <--

US 2004087630 A1 20040506 US 2003-362341 20030618 <--

PRIORITY APPLN. INFO.: US 2000-643642 A 20000822

WO 2001-EP9586 W 20010820

AB The present invention relates to a combination, especially a pharmaceutical composition, comprising (a) an insulin secretion enhancer or a pharmaceutically acceptable salt thereof and (b) at least one of the active ingredients selected from the group consisting of (i) HMG-Co-A reductase inhibitors or a pharmaceutically acceptable salt thereof; and (ii) **ACE inhibitors** or a pharmaceutically acceptable salt thereof; and, in case of a pharmaceutical composition, a pharmaceutically acceptable carrier. Formulations were given as examples, e.g., tablets containing nateglinide.

IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT **Inflammation**

**Intestine, disease**

(**ulcerative colitis**; combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 339-44-6, Glymidine 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6, Glyclopamide 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 3149-00-6, Phenbutamide 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 62571-86-2, Captopril 74258-86-9, Alacepril 75330-75-5, Lovastatin 75847-73-3, Enalapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82834-16-0, Perindopril 83435-66-9, Delapril 83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril 86541-78-8, Benazeprilat 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 98048-97-6, Fosinopril 105816-04-4, Nateglinide 111223-26-8, Ceronapril 111902-57-9, Temocapril 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 145375-43-5, Mitiglinide 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 287714-41-4, Rosuvastatin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors)

L67 ANSWER 28 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:47520 HCAPLUS

DOCUMENT NUMBER: 136:102294

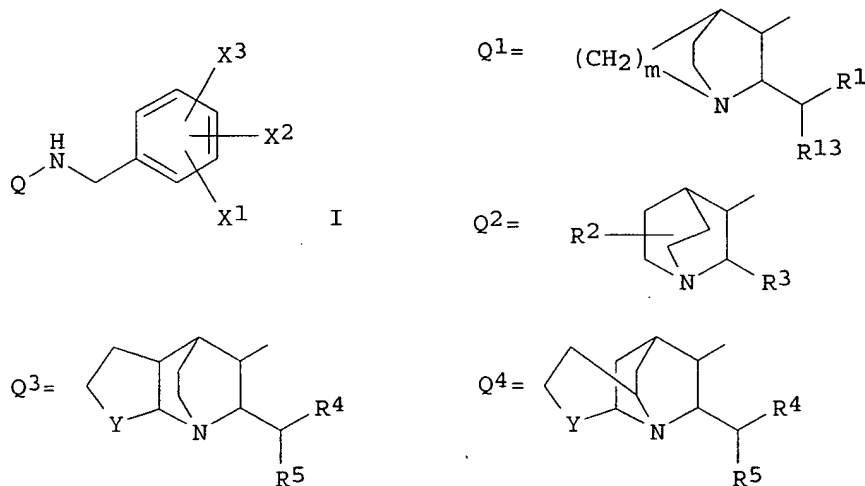
TITLE: Preparation of fluoroalkoxybenzylamino derivatives of nitrogen containing heterocycles as substance P



receptor antagonists  
 INVENTOR(S): Chappel, Phillip Branch; O'Neill, Brian Thomas;  
 Saltarelli, Mario David  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: Eur. Pat. Appl., 44 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1172106	A2	20020116	EP 2001-303983	20010501 <--
EP 1172106	A3	20020515		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ZA 2001003484	A	20021202	ZA 2001-3484	20010430 <--
CA 2345760	AA	20011103	CA 2001-2345760	20010501 <--
JP 2002020287	A2	20020123	JP 2001-134144	20010501 <--
NZ 522391	A	20040827	NZ 2001-522391	20010502 <--
US 2002035147	A1	20020321	US 2001-848069	20010503 <--
US 2003114439	A1	20030619	US 2002-208274	20020729 <--
PRIORITY APPLN. INFO.:			US 2000-201591P	P 20000503
			US 2000-237780P	P 20001004
			NZ 2001-511453	A1 20010502
			US 2001-848069	B1 20010503

OTHER SOURCE(S): MARPAT 136:102294  
 GI



AB The present invention relates to methods of treating various central nervous system (CNS) and other disorders or conditions by administering fluoroalkoxybenzylamino derivs. of nitrogen containing heterocyclic compds., and specifically, by administering compds. of the formula [I; X<sub>1</sub> = H, C<sub>1</sub>-10 alkoxy or alkyl optionally substituted with from one to three fluorine atoms; X<sub>2</sub>, X<sub>3</sub> = halo, H, NO<sub>2</sub>, C<sub>1</sub>-10 alkyl or alkoxy optionally substituted with from one to three fluorine atoms, CF<sub>3</sub>, hydroxy, Ph,

cyano, amino, C1-6 alkylamino, di(C1-6 alkyl)amino, -CONH-C1-6alkyl, C1-6 alkyl-CONH-C1-6 alkyl, hydroxy-C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl, NHCHO, NHCO-C1-C6 alkyl; Q = N-containing heterocyclyl, e.g. Q1, Q2, Q3, Q4; R1 = furyl, thienyl, pyridyl, indolyl, biphenyl, (un)substituted phenyl; R13 = C3-4 branched alkyl, C5-6 branched alkenyl, C5-7 cycloalkyl, groups defined in R1; R2 = H, C1-6 alkyl; R3 = each (un)substituted Ph, biphenyl, naphthyl, pyridyl, benzhydryl, thienyl, or furyl; Y = (CH<sub>2</sub>)<sup>l</sup> (wherein l = an integer from 1 to 3), or cyclohexane-1,2-diyl; Z = O, S, NH, C1-C3 alkyl-NH, (CH<sub>2</sub>)<sup>n</sup> (wherein n = 0, 1, 2); m = 2, 3; R4 = furyl, thienyl, pyridyl, indolyl, biphenyl, (un)substituted phenyl; R5 = thienyl, biphenyl, (un)substituted phenyl] in a mammal. These compds. I are substance P receptor antagonists (no data). The above CNS and other disorders or conditions include sleep disorders, autism, pervasive development disorder, rheumatoid arthritis, osteoarthritis, fibromyalgia, human immunodeficiency virus (HIV) infections, dissociative disorders such as body dysmorphic disorders, eating disorder such as anorexia and bulimia, **ulcerative colitis**, Crohn's disease, irritable bowel syndrome, functional abdominal pain, chronic fatigue syndrome, sudden infant death syndrome (SIDS), overactive bladder, chronic cystitis, chemotherapy induced cystitis, cough, angiotensin converting enzyme (ACE) induced cough, itch, hiccups, premenstrual syndrome, premenstrual dysphoric disorder, schizophrenia, schizoaffective disorder, delusional disorder, substance-induced psychotic disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, schizophreniform disorder, and amenorrheic disorders such as dysmenorrhea. They also include obesity, epilepsy, movement disorders such as primary movement disorders, spasticities, Scott's syndrome, Tourette's syndrome, palsys, amyotrophic lateral sclerosis (ALS), akinetic-rigid disorders, akinesias, dyskinesias, restless leg syndrome and movement disorders associated with Parkinson's disease or Huntington's disease, mastalgia syndromes, motion sickness, immune dysfunctions, generalized anxiety disorder, panic disorder, phobias including social phobia, agoraphobia, and specific phobias, obsessive-compulsive disorder, posttraumatic stress disorder; depression including major depression, single episode depression, recurrent depression, child abuse induced depression, postpartum depression and dysthymia, cyclothymia, bipolar disorder, neurocardiac disorders such as neurocardiac syncope, neurogenic syncope, hypersensitive Carotid sinus, neurovascular syndrome and arrhythmias including arrhythmias secondary to gastrointestinal disturbances, addiction disorders involving addictions to behaviors, HIV-1 associated dementia, AIDS dementia complex, HIV encephalopathy, HIV related neuralgias, AIDS related neuralgias, epilepsy, and attention deficit hyperactivity disorder in a mammal. Thus, reductive alkylation of 2-diphenylmethyl-1-azabicyclo[2.2.2]octan-3-amine by 2-(difluoromethoxy)benzaldehyde using sodium cyanoborohydride in MeOH at room temperature for 30 h gave 2-(Diphenylmethyl)-N-[(2-difluoromethoxy)phenyl]methyl-1-azabicyclo[2.2.2]octan-3-amine.

IC ICM A61K031-445

ICS A61K031-435

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT Cough

(angiotensin converting enzyme-induced; preparation of fluoroalkoxybenzylamino derivs. of nitrogen containing heterocycles as substance P receptor **antagonists** as therapeutic agents)

IT **Inflammation**

**Intestine, disease**

(**ulcerative colitis**; preparation of fluoroalkoxybenzylamino derivs. of nitrogen containing heterocycles as

substance P receptor antagonists as therapeutic agents)  
 IT 9015-82-1, **Angiotensin converting enzyme**  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (cough induced by; preparation of fluoroalkoxybenzylamino derivs. of  
 nitrogen containing heterocycles as substance P receptor  
 antagonists as therapeutic agents)

L67 ANSWER 29 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:868260 HCAPLUS

DOCUMENT NUMBER: 136:627

TITLE: Combinations of enzyme inhibitor-containing  
 preparations and the use in inhibition of mononuclear  
 cells and T-cells and treatment of immune conditions

INVENTOR(S): Ansorge, Siegfried; Arndt, Marco; Buehling, Frank;  
 Lendeckel, Uwe; Neubert, Klaus; Reinhold, Dirk

PATENT ASSIGNEE(S): Institut fuer Medizintechnologie Magdeburg G.m.b.H.  
 IMTM, Germany

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001089569	A1	20011129	WO 2001-EP5887	20010522 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
DE 10025464	A1	20011206	DE 2000-10025464	20000523 <--
CA 2410305	AA	20021122	CA 2001-2410305	20010522 <--
EP 1289559	A1	20030312	EP 2001-945184	20010522 <--
EP 1289559	B1	20050727		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2003534293	T2	20031118	JP 2001-585811	20010522 <--
AT 300313	E	20050815	AT 2001-945184	20010522
US 2005014699	A1	20050120	US 2004-296102	20040326
PRIORITY APPLN. INFO.:			DE 2000-10025464 A	20000523
			WO 2001-EP5887 W	20010522

AB A method is disclosed which permits, owing to the simultaneous and joint **inhibition** of the enzyme activities of (1) alanyl-aminopeptidase and dipeptidyl-peptidase IV, (2) dipeptidyl-peptidase IV and **angiotensin-converting enzyme**, (3) dipeptidyl-peptidase IV and prolyl-oligopeptidase, and (4) dipeptidyl-peptidase IV and X-Pro-aminopeptidase, the **inhibition** of DNA synthesis and thus the proliferation of mononuclear cells and T cells to an extent which cannot be obtained by individual application of the enzyme **inhibitors**, even when used in higher doses. Although the above-mentioned inhibitors influence the same process, namely DNA synthesis and thus the proliferation of immune cells, this effect is not complete and not long-lasting when the inhibitors are used individually.

The functional overlapping of enzymic activities results, as is supported by exptl. data, in an additive/superadditive inhibitory effect on DNA synthesis and the proliferation resulting from the simultaneous inhibition of a plurality of the above enzymes. The invention shows that the simultaneous application of inhibitors of the above enzymes or of corresponding prepsns. and forms of administration is suitable for the therapy of autoimmune diseases and chronic diseases with an inflammatory genesis, as well as for the treatment of post-transplant rejection episodes.

IC ICM A61K045-06  
ICS A61P037-06; A61P035-00; A61K038-55; A61K038-55  
CC 1-7 (Pharmacology)  
ST peptidase **ACE inhibitor** combination immune disorder;  
mononuclear cell antiproliferative peptidase **ACE inhibitor** combination; T cell antiproliferative peptidase **ACE inhibitor** combination; autoimmune disease peptidase **ACE inhibitor** combination; transplant rejection peptidase **ACE inhibitor** combination  
IT Inflammation  
Intestine, disease  
(colitis, colitis ulcerosa; enzyme inhibitor combinations for inhibition of mononuclear cells and T-cells and treatment of immune conditions)  
IT 9015-82-1, Angiotensin-converting enzyme 9054-63-1, Alanyl aminopeptidase 37288-66-7, Aminopeptidase P 54249-88-6, Dipeptidylpeptidase IV 72162-84-6, Prolyl oligopeptidase  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (enzyme inhibitor combinations for inhibition of mononuclear cells and T-cells and treatment of immune conditions)  
IT 72-18-4D, L-Valine, amidated 73-22-3D, L-Tryptophan, amidated 73-32-5D, L-Isoleucine, amidated 147-85-3D, L-Proline, amidated 2577-48-2 3557-90-2D, amidated 13434-13-4, Actinonin 41721-00-0 54164-07-7 56384-04-4 62023-67-0 **62571-86-2**, Captopril 65921-40-6 **75847-73-3**, Enalapril **76547-98-3**, Lisinopril **88768-40-5**, Cilazapril 88795-32-8 99429-59-1 123652-87-9, Probestin 129085-76-3, Leuhistin 135219-43-1, Poststatin 136259-18-2 136259-19-3 136259-20-6 136259-21-7 136259-22-8 136259-23-9 137563-63-4, Eurystatin A 137563-64-5, Eurystatin B 142880-55-5 148152-02-7 160470-73-5, Apstatin 184360-42-7 187402-73-9, Phebestin 192821-27-5 251571-76-3 252860-55-2 252860-56-3 252860-57-4 252860-58-5 327623-45-0 327983-79-9 376346-22-4 376346-23-5 376346-24-6 376346-25-7 376346-26-8 376346-27-9  
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (enzyme inhibitor combinations for inhibition of mononuclear cells and T-cells and treatment of immune conditions)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 30 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:816391 HCAPLUS

DOCUMENT NUMBER: 135:339245

TITLE: Novel tetrazol-biphenyl compounds for the treatment of inflammatory and cardiovascular diseases

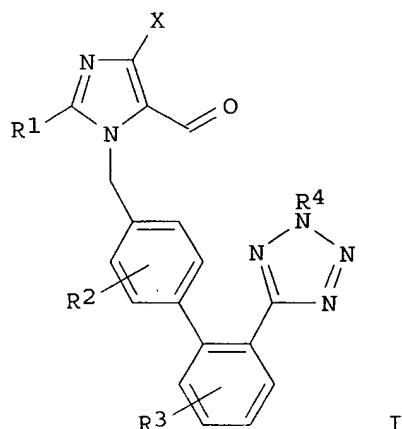
INVENTOR(S): Forssmann, Wolf-Georg; Drexler, Helmut; Walden, Michael; Schieffer, Bernhard; Schmidt, Boris

PATENT ASSIGNEE(S): IPF Pharmaceuticals G.m.b.H., Germany

SOURCE: PCT Int. Appl., 11 pp.

DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082858	A2	20011108	WO 2001-EP5043	20010504 <--
WO 2001082858	A3	20020627		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001067404	A5	20011112	AU 2001-67404	20010504 <--
PRIORITY APPLN. INFO.:			DE 2000-10021615	A 20000504
			WO 2001-EP5043	W 20010504
OTHER SOURCE(S):		MARPAT 135:339245		
GI				



AB The invention concerns a compound having structural formula (I), wherein R1 represents H, substituted or unsubstituted alkyl or acyl groups, especially Me, Et, Pr, iso-Pr, Bu, iso-Bu, tert. Butyl; X = halogen or OH; R2 represents H, substituted or unsubstituted alkyl or acyl groups, especially Me, Et, Pr, iso-Pr, Bu, iso-Bu, tert. Bu, halogen or OH; R3 represents H, substituted or unsubstituted alkyl or acyl groups, especially Me, Et, Pr, iso-Pr, Bu, iso-Bu, tert. Bu, halogen or OH; R4 represents H, substituted or unsubstituted alkyl or acyl groups, especially Me, Et, Pr, iso-Pr, Bu, iso-Bu, tert. Bu or is a metal radical, especially an alkali cation. 2-Butyl-4-chloro-1-[(2'-tetrazol-5-yl)biphenyl-4-yl]methyl-5-(oxomethylene)imidazole can be obtained by the catalytic oxidation of losartan with ruthenium chloride.

IC ICM A61K  
 CC 1-7 (Pharmacology)  
 Section cross-reference(s): 28, 63

ST tetrazol biphenyl deriv antiinflammatory cardiovascular agent **ACE inhibitor**

IT **Intestine, disease**  
(Crohn's; tetrazol-biphenyl compds. for treatment of **inflammatory** and cardiovascular diseases)

IT Alzheimer's disease  
Analgesics  
Anti-inflammatory agents  
Anticoagulants  
Antihypertensives  
Antipyretics  
Antirheumatic agents  
Arthritis  
Cardiovascular agents  
**Celiac disease**  
Dysmenorrhea  
Gout  
Osteoarthritis  
(tetrazol-biphenyl compds. for treatment of inflammatory and cardiovascular diseases)

IT **Intestine, disease**  
(**ulcerative colitis**; tetrazol-biphenyl compds. for treatment of **inflammatory** and cardiovascular diseases)

IT 9015-82-1, **ACE**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**inhibitors** of; tetrazol-biphenyl compds. for treatment of inflammatory and cardiovascular diseases)

L67 ANSWER 31 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:703740 HCAPLUS

DOCUMENT NUMBER: 135:251986

TITLE: Methods for treating fibroproliferative diseases with antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides

INVENTOR(S): Peterson, Theresa C.

PATENT ASSIGNEE(S): Dalhousie University, Can.

SOURCE: U.S., 13 pp., Cont.-in-part of U.S. 6,025,151.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6294350	B1	20010925	US 1999-433621	19991102 <--
US 5985592	A	19991116	US 1997-870096	19970605 <--
US 6025151	A	20000215	US 1998-92317	19980605 <--
WO 2001032156	A2	20010510	WO 2000-IB1731	20001102 <--
WO 2001032156	A3	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

## PRIORITY APPLN. INFO.:

US 1997-870096 A2 19970605  
US 1998-92317 A2 19980605  
US 1999-433621 A1 19991102

AB In accordance with the present invention, fibroproliferative disease or condition characterized by such symptoms as increased levels of c-Jun homodimers, increased heterodimerization of c-Jun with another signaling peptide, increased levels of phosphorylated c-Jun, or increased presence of Jun kinase are treated by administering to the subject an amount of a compound effective to ameliorate one or more of the symptoms of the disease or condition, for example, an antiproliferative or antifibrotic agent. Preferred compds. for administration according to the invention are antisense c-Jun oligonucleotides and compds. that block c-Jun phosphorylation, such as pentoxifylline, or a functional derivative or metabolite thereof. Also provided by the present invention are in vitro tests for identifying whether a test compound is useful for treatment of a subject afflicted with such a disease and kits useful for conducting such assays.

IC ICM C12Q001-02

ICS C12Q001-00; C12Q001-50

INCL 435029000

CC 1-12 (Pharmacology)

Section cross-reference(s): 9, 63

IT **Intestine, disease**

(**inflammatory**; antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 50-23-7, Hydrocortisone 54-85-3, Isoniazid 54-85-3D, Isoniazid, conjugated 59-67-6, Niacin, biological studies 64-86-8, Colchicine 107-35-7, Taurine 518-34-3, Tetrandrine 1028-33-7, Pentifylline 1405-86-3, Glycyrrhizin 6493-05-6, Pentoxifylline 6493-05-6D, Pentoxifylline, derivs. and metabolites 6493-06-7, 1H-Purine-2,6-dione, 3,7-dihydro-1-(5-hydroxyhexyl)-3,7-dimethyl- 10102-43-9, Nitric oxide, biological studies 53179-13-8, Pirfenidone 55242-55-2, Propentofylline 55837-20-2, Halofuginone 62571-86-2, Captopril 75847-73-3, Enalapril 80288-49-9, Furafllyline 83150-76-9, Octreotide 85721-33-1, Ciprofloxacin 91161-71-6, Terbinafine 114798-26-4, Losartan 119290-87-8, Acanthoic acid 120210-48-2, Tenidap  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT 9015-82-1, **Angiotensin converting enzyme**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**inhibitors**; antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 32 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:452872 HCAPLUS

DOCUMENT NUMBER: 135:56494

TITLE: Methods for treating and preventing damage to mucosal tissue using angiotensinogen, angiotensin I, AI analogs, AI fragments and analogs, angiotensin II, AII analogs, AII fragments or analogs or AII AT2 type 2 receptor agonists

INVENTOR(S): Rodgers, Kathleen E.; Dizerega, Gere S.

PATENT ASSIGNEE(S): University of Southern California, USA  
 SOURCE: PCT Int. Appl., 45 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001043761	A2	20010621	WO 2000-US32141	20001127 <--
WO 2001043761	A3	20020307		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2393755	AA	20010621	CA 2000-2393755	20001127 <--
AU 2001017931	A5	20010625	AU 2001-17931	20001127 <--
EP 1239867	A2	20020918	EP 2000-980704	20001127 <--
EP 1239867	B1	20050126		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517019	T2	20030520	JP 2001-544898	20001127 <--
US 6821953	B1	20041123	US 2000-723257	20001127 <--
AT 287724	E	20050215	AT 2000-980704	20001127
US 2005004036	A1	20050106	US 2004-875155	20040623
PRIORITY APPLN. INFO.:				
			US 1999-171249P	P 19991216
			US 2000-213224P	P 20000619
			US 2000-723257	A1 20001127
			WO 2000-US32141	W 20001127

OTHER SOURCE(S): MARPAT 135:56494

AB The present invention provides improved methods, kits, and pharmaceutical compns. for treating and preventing damage to mucosal tissue by administering an effective amount of angiotensinogen, angiotensin I (AI), AI analogs, AI fragments and analogs thereof, angiotensin II (AII), AII analogs, AII fragments or analogs thereof or AII AT2 type 2 receptor agonists to the subject. Administration of anti-inflammatory drugs, **angiotensin converting enzyme inhibitors**, anti-infectives, growth factors, and/or antihistamines in combination with the above compns. is also claimed.

IC ICM A61K038-00

CC 2-10 (Mammalian Hormones)

IT **Intestine, disease**

(**ulcerative colitis**, non-specific inflammations; methods for treating and preventing damage to mucosal tissue using angiotensinogen, AI, AI analogs, AI fragments and analogs, AII, AII analogs, AII fragments or analogs or AII AT2 type 2 receptor agonists)

IT 9015-82-1, **Angiotensin converting enzyme**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**inhibitor**; methods for treating and preventing damage to mucosal tissue using angiotensinogen, AI, AI analogs, AI fragments and analogs, AII, AII analogs, AII fragments or analogs or AII AT2 type 2



receptor agonists)

L67 ANSWER 33 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:427871 HCAPLUS

DOCUMENT NUMBER: 135:266468

TITLE: Fish oil - a potential therapy for inflammatory atherosclerosis

AUTHOR(S): Saldeen, Tom; Mehta, Jay L.

CORPORATE SOURCE: Department of Surgical Sciences, University of Uppsala, Uppsala, 752 37, Swed.

SOURCE: Inflammatory and Infectious Basis of Atherosclerosis (2001), 243-257. Editor(s): Mehta, Jay L. Birkhaeuser Verlag: Basel, Switz.

CODEN: 69BJTK

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review with 70 refs. Inflammation plays an important role in both the initiation of atherosclerosis and the development of atherothrombotic events. An anti-inflammatory effect of n-3 fatty acids in fish oil was suggested by epidemiol. studies which show that Greenland Eskimos, who consume large quantities of fish oils rich in long-chain n-3 fatty acids, have a very low incidence not only of atherosclerosis and coronary artery disease but also of inflammatory and autoimmune disorders such as rheumatoid arthritis, psoriasis, asthma, **inflammatory bowel disease**, type I diabetes mellitus, thyrotoxicosis and multiple sclerosis. Fifteen large studies enrolling more than 60,000 subjects have shown a decreased mortality in CAD as well as in total mortality of about 20-30% after intake of fish oil, fatty fish or n-3 fatty acids. In a randomized controlled trial on the effect of intake of fatty fish or natural fish oil, 2033 men who had recovered from myocardial infarction were studied for two years. The fish/fish oil group showed a 29% reduction in two year all-cause mortality. In another study enrolling 11,324 patients surviving a recent myocardial infarction, intake of 1 g daily of n-3 fatty acids in 2,836 patients for 3.5 yr resulted in a 20% decrease in total deaths, a 30% decrease in cardiovascular deaths and a 45% decrease in sudden deaths. Interestingly, these patients already had conventional treatment with aspirin, beta-blockers and **angiotensin converting enzyme inhibitors** and were already exposed to a healthy Mediterranean diet. Thus, there seems to be no doubt that fish oil has a beneficial effect on CAD. Stable fish oil has many interesting effects suggesting a major role for this oil as a potential therapy for inflammatory atherosclerosis.

CC 1-0 (Pharmacology)

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 34 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:338333 HCAPLUS

DOCUMENT NUMBER: 134:357558

TITLE: Methods for treating fibroproliferative diseases

INVENTOR(S): Peterson, Theresa C.

PATENT ASSIGNEE(S): Dalhousie University, Can.

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032156	A2	20010510	WO 2000-IB1731	2000,1102 <--
WO 2001032156	A3	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6294350	B1	20010925	US 1999-433621	19991102 <--
PRIORITY APPLN. INFO.:			US 1999-433621	A1 19991102
			US 1997-870096	A2 19970605
			US 1998-92317	A2 19980605
AB	In accordance with the present invention, fibroproliferative disease or condition characterized by such symptoms as increased levels of c-Jun homodimers, increased heterodimerization of c-Jun with another signaling peptide, increased levels of phosphorylated c-Jun, or increased presence of Jun kinase are treated by administering to the subject an amount of a compound effective to ameliorate one or more of the symptoms of the disease or condition, for example, an antiproliferative or antifibrotic agent. Preferred compds. for administration according to the invention are antisense c-Jun oligonucleotides and compds. that block c-Jun phosphorylation, such as pentoxifylline, or a functional derivative or metabolite thereof. Also provided by the present invention are in vitro tests for identifying whether a test compound is useful for treatment of a subject afflicted with such a disease and kits useful for conducting such assays.			
IC	ICM A61K031-00 ICS A61K031-522; A61K045-00; A61K045-06; A61K048-00; C12Q001-48; G01N033-58; A61P019-04; A61P035-00; A61P037-00; A61P025-28; A61P043-00; A61P033-06; A61P031-12; A61P039-00; A61P035-02; A61P001-00; A61P011-00; A61P013-12; A61P009-00			
CC	63-6 (Pharmaceuticals) Section cross-reference(s): 1, 2, 8, 15			
IT	<b>Intestine, disease</b> (inflammatory; antisense oligonucleotide preps. for treating fibroproliferative diseases)			
IT	50-23-7, Hydrocortisone 54-85-3, Isoniazid 59-67-6, Niacin, biological studies 64-86-8, Colchicine 107-35-7, Taurine 518-34-3, Tetrandrine 1028-33-7, Pentifylline 1405-86-3, Glycyrrhizin 6493-05-6, Pentoxifylline 6493-06-7 10102-43-9, Nitric oxide, biological studies 53179-13-8, Pirfenidone 55242-55-2, Propentofylline 55837-20-2, Halofuginone 62571-86-2, Captopril 75847-73-3, Enalapril 80288-49-9, Furafllyline 83150-76-9, Octreotide 85721-33-1, Ciprofloxacin 91161-71-6, Terbinafine 114798-26-4, Losartan 119290-87-8, Acanthoic acid 120210-48-2, Tenidap RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antisense oligonucleotide preps. for treating fibroproliferative diseases)			
IT	9015-82-1, <b>Angiotensin converting enzyme</b> RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; antisense oligonucleotide preps. for treating fibroproliferative diseases)			

L67 ANSWER 35 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:790293 HCAPLUS

DOCUMENT NUMBER: 133:344615

TITLE: ACE-2 inhibiting compounds, their preparation, pharmaceutical compositions containing them, and their therapeutic use

INVENTOR(S): Acton, Susan L.; Ocain, Timothy D.; Gould, Alexandra E.; Dales, Natalie A.; Guan, Bing; Brown, James A.

PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 127 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066104	A2	20001109	WO 2000-US11550	20000428 <--
WO 2000066104	A3	20010628		
WO 2000066104	C2	20020829		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2372387	AA	20001109	CA 2000-2372387	20000428 <--
EP 1183019	A2	20020306	EP 2000-926478	20000428 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103094	T2	20020321	TR 2001-200103094	20000428 <--
BR 2000010166	A	20020604	BR 2000-10166	20000428 <--
JP 2002543120	T2	20021217	JP 2000-614989	20000428 <--
US 6632830	B1	20031014	US 2000-561759	20000428 <--
NO 2001005274	A	20011228	NO 2001-5274	20011029 <--
ZA 2001009378	A	20021114	ZA 2001-9378	20011114 <--
PRIORITY APPLN. INFO.:			US 1999-132034P	P 19990430
			US 1999-171052P	P 19991216
			WO 2000-US11550	W 20000428

OTHER SOURCE(S): MARPAT 133:344615

AB ACE-2 inhibiting compds. are disclosed. Methods of using the compds. and pharmaceutical compns. containing the compds. are also claimed. The compds. of the invention are useful for treating e.g. blood pressure-related diseases. Compound preparation is described.

IC ICM A61K031-00

CC 1-8 (Pharmacology)

Section cross-reference(s): 34, 63

ST ACE2 inhibitor prepn therapeutic; blood pressure disease ACE2 inhibitor; **angiotensin converting enzyme 2 inhibitor** therapeutic

IT **Intestine, disease**

(**inflammatory**; ACE-2 inhibitor preparation, pharmaceutical compns., and therapeutic use)

IT 1407-47-2, Angiotensin 9015-82-1, **Angiotensin-**

converting enzyme 9041-90-1, Angiotensin I 11075-17-5,  
 Carboxypeptidase A 23827-88-5, 2-8-Bradykinin 23828-06-0,  
 2-7-Bradykinin 55508-42-4, Neurotensin(1-13) 63529-99-7,  
 Neurotensin(1-12) 189696-01-3 305336-82-7 305336-84-9  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (ACE-2 inhibitor preparation, pharmaceutical compns., and  
 therapeutic use)

L67 ANSWER 36 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:688272 HCAPLUS

DOCUMENT NUMBER: 133:280563

TITLE: Human antibodies that bind human IL-12 and methods for  
 producing

INVENTOR(S): Salfeld, Jochen G.; Roguska, Michael; Paskind,  
 Michael; Banerjee, Subhashis; Tracey, Daniel E.;  
 White, Michael; Kaymakcalan, Zehra; Labkovsky, Boris;  
 Sakorafas, Paul; Friedrich, Stuart; Myles, Angela;  
 Veldman, Geertruida M.; Venturini, Amy; Warne,  
 Nicholas W.; Widom, Angela; Elvin, John G.; Duncan,  
 Alexander R.; Derbyshire, Elaine J.; Carmen, Sara;  
 Smith, Stephen; Holtet, Thor Las; Du, Fou Sarah L.  
 PATENT ASSIGNEE(S): Basf A.-G., Germany; Genetics Institute Inc.; et al.  
 SOURCE: PCT Int. Appl., 377 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056772	A1	20000928	WO 2000-US7946	20000324 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2365281	AA	20000928	CA 2000-2365281	20000324 <--
NZ 513945	A	20010928	NZ 2000-513945	20000324 <--
BR 2000009323	A	20020108	BR 2000-9323	20000324 <--
EP 1175446	A1	20020130	EP 2000-918396	20000324 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
TR 200102715	T2	20020923	TR 2001-200102715	20000324 <--
JP 2002542770	T2	20021217	JP 2000-606632	20000324 <--
US 6914128	B1	20050705	US 2000-534717	20000324
ZA 2001007774	A	20021220	ZA 2001-7774	20010920 <--
NO 2001004605	A	20011126	NO 2001-4605	20010921 <--
BG 106027	A	20020628	BG 2001-106027	20011018 <--
NZ 529571	A	20031219	NZ 2003-529571	20031117 <--
US 2005004354	A1	20050106	US 2004-884830	20040701
PRIORITY APPLN. INFO.:			US 1999-126603P	P 19990325
			US 2000-534717	A3 20000324
			WO 2000-US7946	W 20000324

AB Human antibodies, preferably recombinant human antibodies, that specifically bind to human interleukin-12 (hIL-12) are disclosed. Preferred antibodies have high affinity for hIL-12 and neutralize hIL-12 activity in vitro and in vivo. An antibody of the invention can be a full-length antibody or an antigen-binding portion thereof. The antibodies, or antibody portions, of the invention are useful for detecting hIL-12 and for inhibiting hIL-12 activity, e.g., in a human subject suffering from a disorder in which hIL-12 activity is detrimental. Nucleic acids, vectors and host cells for expressing the recombinant human antibodies of the invention, and methods of synthesizing the recombinant human antibodies, are also encompassed by the invention.

IC ICM C07K016-24  
ICS C12N015-13; C12N015-63; C12N005-10; C07K016-00; A61K039-395; G01N033-577; C12P021-08; A61P043-00

CC 15-3 (Immunochemistry)  
Section cross-reference(s): 3

IT **Intestine, disease**  
(Crohn's; recombinant human antibodies that bind human IL-12 for treatment of autoimmune diseases and **inflammatory** diseases)

IT **Intestine, disease**  
(**inflammatory**; recombinant human antibodies that bind human IL-12 for treatment of autoimmune diseases and **inflammatory** diseases)

IT **Intestine, disease**  
(**ulcerative colitis**; recombinant human antibodies that bind human IL-12 for treatment of autoimmune diseases and **inflammatory** diseases)

IT 9004-06-2, Elastase 9015-82-1, **Angiotensin converting** enzyme 9025-82-5, Phosphodiesterase 9029-60-1, Lipoxxygenase 122191-40-6, Interleukin 1 $\beta$  converting enzyme 151769-16-3, TNF $\alpha$  converting enzyme  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**inhibitors**; recombinant human antibodies that bind human IL-12 for treatment of autoimmune diseases and inflammatory diseases)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 37 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2000:534969 HCAPLUS  
DOCUMENT NUMBER: 133:140262  
TITLE: Slow-release pharmaceutical compositions  
INVENTOR(S): Huber, Gerald; Gruber, Peter  
PATENT ASSIGNEE(S): Losan Pharma G.m.b.H., Germany  
SOURCE: PCT Int. Appl., 49 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044353	A1	20000803	WO 1999-IB180	19990129 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW			

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2360655	AA	20000803	CA 1999-2360655	19990129 <--
AU 9919808	A1	20000818	AU 1999-19808	19990129 <--
AU 764469	B2	20030821		
EP 1146862	A1	20011024	EP 1999-900623	19990129 <--
EP 1146862	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9916972	A	20011106	BR 1999-16972	19990129 <--
JP 2002535353	T2	20021022	JP 2000-595657	19990129 <--
AT 238040	E	20030515	AT 1999-900623	19990129 <--
NZ 513037	A	20030530	NZ 1999-513037	19990129 <--
PT 1146862	T	20030930	PT 1999-900623	19990129 <--
ES 2197600	T3	20040101	ES 1999-900623	19990129 <--
NO 2001003336	A	20010925	NO 2001-3336	20010705 <--
US 6962717	B1	20051108	US 2001-890104	20011016

PRIORITY APPLN. INFO.:

EP 1999-900623 A 19990129  
WO 1999-IB180 A 19990129

AB A pharmaceutical composition for the slow release of an active agent in the gastrointestinal tract comprises multiple particles which contain an active agent and which are coated with a material that is insol. in gastrointestinal juice. The particles have a core consisting of a homogeneous mixture of pharmaceutical active agent and a polymer which is insol. in gastrointestinal juice, with a maximum average inner pore diameter of 35

µm. The composition enables an efficient release which is independent of pH, even with comparatively small quantities of polymer, and has good stability during storage. Thus, a mixture of 5-aminosalicylic acid (I) 175, Eudragit RS30D 29.167, and tri-Et citrate 1.750 kg was granulated with 7.65 kg H<sub>2</sub>O, dried at 50-90°, compacted, coated with a suspension containing Eudragit NE40D 20.869, talc 4.435, 33% simethicone antifoam emulsion 0.509, and H<sub>2</sub>O 20.867 kg, and 198.450 kg of the coated granules (maximum size 1000 µm) were mixed with microcryst. cellulose 50.421, Kollidon K90 3.129, and Kollidon CL 14.000 kg in a cyclone granulator and compressed into 760-mg tablets each containing 500.00 mg I. These tablets released 24.9 and 82.5% of their I content after 30 and 240 min, resp., at pH 1.2.

IC ICM A61K009-16

ICS A61K009-50; A61K009-00; A61K009-20; A61K009-48

CC 63-6 (Pharmaceuticals)

IT Intestine, disease

(ulcerative colitis; slow-release pharmaceutical compns.)

IT 52-26-6, Morphine hydrochloride 57-27-2, Morphine, biological studies 89-57-6, 5-Aminosalicylic acid 26787-78-0, Amoxicillin 27203-92-5, Tramadol 36282-47-0, Tramadol hydrochloride 51333-22-3, Budesonide 58001-44-8, Clavulanic acid 59277-89-3, Acyclovir 66357-35-5, Ranitidine 73590-58-6, Omeprazole 75847-73-3, Enalapril 76824-35-6, Famotidine 79902-63-9, Simvastatin 81093-37-0, Pravastatin 88150-42-9, Amlodipine  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(slow-release pharmaceutical compns.)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 38 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:144772 HCAPLUS  
 DOCUMENT NUMBER: 132:189689  
 TITLE: Bioreductive conjugates for drug targeting  
 INVENTOR(S): Adams, Ged; Blake, David; Naughton, Declan; Stratford, Ian  
 PATENT ASSIGNEE(S): Theramark Limited, UK; Adams, Margaret  
 SOURCE: PCT Int. Appl., 48 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010610	A2	20000302	WO 1999-GB2606	19990819 <--
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9954296	A1	20000314	AU 1999-54296	19990819 <--
PRIORITY APPLN. INFO.:			GB 1998-18027	A 19980819
			GB 1998-18156	A 19980820
			WO 1999-GB2606	W 19990819

OTHER SOURCE(S): MARPAT 132:189689

AB The use of a bioreductive conjugate comprised of a noncytotoxic bioreductive moiety having linked thereto at least one therapeutic agent, and salts thereof, is disclosed for the healing of wounds and the treatment of fibrotic disorders, **ulcerative colitis**, **inflammatory bowel disease**, epilepsy, cardiovascular reperfusion injury, cerebral reperfusion injury, hypertension, cystic fibrosis, psoriasis, para-psoriasis, peptic ulcers, gastric ulcers, duodenal ulcers, diabetic ulcers dementia, oncol., AIDS, rheumatoid arthritis, diabetes, and ischemia. Various specific conjugates for treating these conditions are also disclosed.

IC ICM A61K047-48

CC 1-12 (Pharmacology)

IT **Intestine, disease**

(**inflammatory**; bioreductive conjugates for drug targeting)

IT **Stomach, disease**

(**ulcer**; bioreductive conjugates for drug targeting)

IT **Intestine, disease**

(**ulcerative colitis**; bioreductive conjugates for drug targeting)

IT 50-06-6D, Phenobarbitone, conjugates, biological studies 50-24-8D,  
 Prednisolone, conjugates 50-78-2D, Aspirin, conjugates 52-53-9D,  
 Verapamil, conjugates 52-67-5D, Penicillamine, conjugates 53-86-1D,  
 Indomethacin, conjugates 57-41-0D, Phenytoin, conjugates 58-32-2D,  
 Dipyridamole, conjugates 59-05-2D, Methotrexate, conjugates 66-97-7D,  
 Psoralen, conjugates 89-57-6D, Mesalazine, conjugates 89-57-6D,  
 5-Aminosalicylic acid, derivs., conjugates 118-42-3D,  
 Hydroxychloroquine, conjugates 305-03-3D, Chlorambucil, conjugates  
 443-48-1D, Metronidazole, conjugates 446-86-6D, Azathioprine, conjugates  
 599-79-1D, Sulfasalazine, conjugates 1069-66-5D, Sodium valproate,

conjugates 1406-16-2D, Vitamin D, analogs, conjugates 6556-11-2D, Inositol nicotinate, conjugates 12244-57-4D, Myochrysine, conjugates 15307-86-5D, Diclofenac, conjugates 15687-27-1D, Ibuprofen, conjugates 21829-25-4D, Niphedipine, conjugates 22204-53-1D, Naproxen, conjugates 26171-23-3D, Tolmetin, conjugates 29679-58-1D, Fenoprofen, conjugates 38194-50-2D, Sulindac, conjugates 51234-28-7D, Benoxaprofen, conjugates 56180-94-0D, Acarbose, conjugates 59865-13-3D, Cyclosporin A, conjugates 62571-86-2D, Captopril, conjugates 67763-97-7D, Insulin-like growth factor II, conjugates 73590-58-6D, Omeprazole, conjugates 79217-60-0D, Cyclosporin, derivs., conjugates 87333-19-5D, Ramipril, conjugates 87679-37-6D, Trandolapril, conjugates 97240-79-4D, Topiramate, conjugates 103577-45-3D, Lansoprazole, conjugates 113194-81-3, TMK 209 117976-89-3D, Rabeprazole, conjugates 259876-40-9, TMK 210 259876-41-0, TMK 207  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(bioreductive conjugates for drug targeting)

IT 9015-82-1, **Angiotensin-converting** enzyme 9025-82-5, Phosphodiesterase 9036-21-9, Phosphodiesterase IV 9055-65-6, Prostaglandin synthetase 9068-52-4, Phosphodiesterase V 81669-70-7, Metalloprotease 99676-46-7, Kexin 125978-95-2, Nitric oxide synthase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; bioreductive conjugates for drug targeting)

L67 ANSWER 39 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:573330 HCAPLUS

DOCUMENT NUMBER: 132:91438

TITLE: Lipid peroxidation and tissue damage

AUTHOR(S): Mylonas, Chrisostomos; Kouretas, Demetrios

CORPORATE SOURCE: Department of Pharmacology, University of Leeds, Leeds, LS2 9JT, UK

SOURCE: In Vivo (1999), 13(3), 295-309

CODEN: IVIVE4; ISSN: 0258-851X

PUBLISHER: International Institute of Anticancer Research

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB Review with 56 refs. In recent years it has become apparent that the oxidation of lipids, or lipid peroxidn., is a crucial step in the pathogenesis of several disease states in adult and infant patients. Lipid peroxidn. is a process generated naturally in small amts. in the body, mainly by the effect of several reactive oxygen species (hydroxyl radical, hydrogen peroxide etc.). It can also be generated by the action of several phagocytes. These reactive oxygen species readily attack the polyunsatd. fatty acids of the fatty acid membrane, initiating a self-propagating chain reaction. The destruction of membrane lipids and the end-products of such lipid peroxidn. reactions are especially dangerous for the viability of cells, even tissues. Enzymic (catalase, superoxide dismutase) and nonenzymic (vitamins A and E) natural antioxidant defense mechanisms exist; however, these mechanisms may be overcome, causing lipid peroxidn. to take place. Since lipid peroxidn. is a self-propagating chain-reaction, the initial oxidation of only a few lipid mols. can result in significant tissue damage. Despite extensive research in the field of lipid peroxidn. it has not yet been precisely determined if it is the cause or an effect of several pathol. conditions. Lipid peroxidn. has been implicated in disease states such as atherosclerosis, **inflammatory bowel** disease, retinopathy of prematurity, bronchopulmonary dysplasia, asthma, Parkinson's disease, kidney damage, preeclampsia and others.



CC 14-0 (Mammalian Pathological Biochemistry)  
 Section cross-reference(s): 13  
 IT **Intestine, disease**  
 (inflammatory; lipid peroxidn. and its relation to tissue  
 damage in different pathol. states)  
 IT 73-31-4, Melatonin **62571-86-2**, Captopril  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antioxidant; lipid peroxidn. and its relation to tissue damage in  
 different pathol. states)  
 REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 40 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1998:453581 HCAPLUS  
 DOCUMENT NUMBER: 129:215128  
 TITLE: The pathogenetic role of endogenous angiotensin II in  
 stress ulcer in obstructive jaundice rats  
 AUTHOR(S): Mou, Dongcheng; Zhu, Xueguang; Xu, Wei; Du, Ruyu  
 CORPORATE SOURCE: Department of Surgery, Sichuan People's Hospital,  
 Chengdu, 610072, Peop. Rep. China  
 SOURCE: Chinese Medical Journal (Beijing, English Edition) (   
 1998), 111(4), 309-312  
 CODEN: CMJODS; ISSN: 0366-6999  
 PUBLISHER: Chinese Medical Association  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The aim was to investigate the pathogenetic role of endogenous  
**angiotensin II** (Ang II) in the mechanism of stress ulcer in  
 obstructive jaundice rats and to detect the effect of **angiotensin**  
**converting enzyme inhibitor** (ACEI) on stress ulcer in  
 obstructive jaundice rats. After common bile duct ligation (CBDL) in  
 Wistar rats, the content of plasma and gastric mucosal Ang II, gastric  
 mucosal blood flow (GMBF) and gastric mucosal damage were measured, and  
 the relation among them was analyzed. The plasma Ang II contents  
 increased much more significantly at 1, 3, 7 and 14 days following CBDL  
 than those in non-CBDL rats. Within 120 min following cold-restraint  
 stress, plasma and gastric mucosal Ang II contents were elevated, GMBF  
 decreased, and ulcer index and gastric mucosal damage increased more  
 significantly than those in non-cold-restraint stress rats.  
 Administration of an ACEI, enalapril, to CBDL rats (5 mg·kg-  
 1·day-1, orally for two days) before stress reduced both the plasma  
 and gastric mucosal Ang II levels, inhibited the decrease of GMBF and  
 decreased ulcer index and gastric mucosal damage. The endogenous Ang II  
 plays a significant pathogenetic role in the development of stress ulcer  
 in obstructive jaundice rats, and ACEI may prevent stress ulcer.

CC 14-7 (Mammalian Pathological Biochemistry)  
 Section cross-reference(s): 1, 2  
 ST angiotensin II stress ulcer obstructive jaundice; **ACE**  
**inhibitor** stress ulcer angiotensin II  
 IT Blood plasma  
 (angiotensin II; pathogenetic role of endogenous  
**angiotensin II** in stress ulcer in obstructive jaundice rats in  
 relation to **angiotensin converting enzyme**  
**inhibitor**)  
 IT Stress, animal  
 (cold-restraint; pathogenetic role of endogenous **angiotensin**  
**II** in stress ulcer in obstructive jaundice rats in relation to  
**angiotensin converting enzyme inhibitor**)  
 IT Circulation

(gastric mucosal; pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

IT Stomach

(mucosa, **angiotensin II** and blood flow; pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

IT Jaundice

(obstructive; pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

IT Antiulcer agents

(pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

IT Stress, animal

(restraint, cold-restraint stress; pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

IT Stomach, disease

(ulcer, stress; pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

IT 9015-82-1

RL: BSU (Biological study, unclassified); BIOL (Biological study) (**inhibitors**; pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

IT 9015-82-1, **Angiotensin converting enzyme**

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

IT 11128-99-7, **Angiotensin II**

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

IT 75847-73-3, Enalapril

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pathogenetic role of endogenous **angiotensin II** in stress ulcer in obstructive jaundice rats in relation to **angiotensin converting enzyme inhibitor**)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 41 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:138222 HCAPLUS

DOCUMENT NUMBER: 126:229452

TITLE: The rationale for peptide drug delivery to the colon and the potential of polymeric carriers as effective tools

AUTHOR(S): Rubinstein, Abraham; Tirosh, Boaz; Baluom, Muhammad; Nassar, Taher; David, Ayelet; Radai, Raphael; Gliko-Kabir, Irit; Friedman, Michael

CORPORATE SOURCE: The Hebrew University of Jerusalem, School of Pharmacy, The David R. Bloom Center of Pharmacy, P.O. Box 12065, Jerusalem, Israel

SOURCE: Journal of Controlled Release (1997), 46(1,2), 59-73  
CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 111 refs. The explicit use of colon-specific drug delivery systems is for the local treatment of colon diseases such as **ulcerative colitis**. Some efficient therapeutic systems, primarily prodrugs and polymeric carriers of salicylate derivs., have been developed and commercialized during the past 20 yr. Speculating that the colon is a superior organ for peptide drug absorption after oral ingestion, many studies indicate that colon-specific drug carriers may potentially be used for the delivery of peptide drugs to that organ. This notion stems from the assumption that the overall proteolytic activity in the colon is lower than and different from the proteolytic activity in the small intestine, e.g., the degradation rate of albumin, azo-albumin casein, azo-casein and collagen in human ileal effluent was faster than the degradation rate in fecal slurries. Other studies, in which the degradation rates

of insulin and insulin B-chain in the small and large intestine of the guinea pig were compared, showed higher degradation rates in the small intestine. It is noteworthy, however, that a peptide drug may stay much longer (up to 10-fold longer) in the large intestine. Thus, even if the enzymic activity is lower, the drug is exposed longer to proteolytic activity. Yet, if the drug is properly protected or formulated with absorption enhancers, the prolonged residence time may increase drug absorption from the large intestine. Thus, prolonged drug blood levels of the **ACE inhibitors** benazepril and captopril have been demonstrated in a number of studies after colonic administration to rats and dogs. A possible explanation for the 'flat' pharmacokinetic profiles obtained may be the 'closed compartment conditions' existing in the colon resulting from the extremely slow propulsive movement of digesta in that organ. These almost stationary conditions may also benefit the performance of functional adjuvants, such as absorption enhancers or peptidase inhibitors, because their dilution rate with the luminal contents of the colon is low. For the purpose of colon-specific drug delivery a variety of polymers has been developed, including acrylic polymers modified with azo crosslinkers and saccharide polymers. Both kinds have been tested in vitro and in animal studies for their ability to be degraded specifically by typical enzymes of the colon. In addition, swellable polymers were utilized in new pulsatile and delayed-release colonic delivery systems after being protected with enteric coating polymers. To secure peptide drugs in the GI tract, especially in the colon,

the

use of cross-linked acrylic acid derivs. such as polycarbophil and Carbopol 934 has also been suggested. New biodegradable polymers and polymers with controllable swelling properties can be used for the specific delivery of drugs to the colon. Furthermore, some polymers, by virtue of their intrinsic proteolytic inhibition properties, could be used

to improve the absorption of peptide drugs from colonic delivery systems.

CC 63-0 (Pharmaceuticals)

Section cross-reference(s): 1, 2

L67 ANSWER 42 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:480039 HCAPLUS

DOCUMENT NUMBER: 121:80039

TITLE: Protective effects of the inhibition of the  
renin-angiotensin system against gastric mucosal  
lesions induced by cold-restraint in the rat

AUTHOR(S): Ender, F.; Labancz, T.; Rosivall, L.

CORPORATE SOURCE: Dep. Surg. SCHOPF-MEREI Hosp., SEMMEL WEIS Univ. Med.  
Sch., BUDAPEST, Hung.

SOURCE: Acta Physiologica Hungarica (1993), 81(1),  
13-18

CODEN: APHHDU; ISSN: 0231-424X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Expts. were designed to examine whether inhibition of the  
renin-angiotensin system alters gastric mucosal damage in conscious rats  
subjected to restraint. Two hours immobilization resulted in an ulcer  
index of  $46 \pm 4$  ( $n = 16$ ) which was decreased by converting enzyme  
inhibitor (MK 422, enalaprilat) doses of 1 and 10 mg·kg<sup>-1</sup>·h<sup>-1</sup>  
by  $50 \pm 16$  ( $n = 8$ ) and  $66 \pm 8\%$  ( $n = 13$ ), resp. ( $p < 0.05$ ).  
Gastric blood flow measured by both the <sup>99</sup>Tc-labeled frog erythrocytes and  
86Rb-clearance methods was low in untreated rats and increased to more  
than three-fold in **angiotensin converting enzyme**  
**inhibitor** treated animals. Infusion of saralasin a specific  
angiotensin II receptor blocker (5 µg·kg<sup>-1</sup>·h<sup>-1</sup>,  $n = 25$ )  
also decreased the ulcer index by  $40 \pm 5\%$  ( $p < 0.05$ ). Thus inhibition  
of the renin-angiotensin system in conscious cold-restraint rat increased  
gastric blood flow and reduced mucosal damage. These results suggest that  
the renin-angiotensin system plays a significant role in the development  
of exptl. gastric ulcer in the cold-restraint model.

CC 14-7 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 1

ST stress **stomach ulcer** pathogenesis renin angiotensin;  
enalaprilat stress **stomach ulcer** inhibition; saralasin  
stress **stomach ulcer** inhibition

IT Stress, biological  
(**stomach ulceration** from, renin-angiotensin system  
in)

IT Receptors  
RL: BIOL (Biological study)  
(angiotensin II, in stress-induced **stomach ulceration**  
)

IT 9015-94-5, Renin, biological studies  
RL: BIOL (Biological study)  
(-angiotensin system, in stress-induced **stomach**  
**ulceration**)

IT 1407-47-2, Angiotensin  
RL: BIOL (Biological study)  
(-renin system, in stress-induced **stomach ulceration**  
)

IT 9015-82-1, **Angiotensin converting enzyme**  
RL: BIOL (Biological study)  
(**inhibition** of, stress-induced **stomach**  
**ulceration** prevention by)

IT 11128-99-7, Angiotensin

RL: BIOL (Biological study)  
(receptors for, in stress-induced **stomach ulceration**  
)

IT 34273-10-4, Saralasin **76420-72-9**, Enalaprilat

RL: BIOL (Biological study)  
(stress-induced **stomach ulceration** prevention by)

L67 ANSWER 43 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:656016 HCAPLUS

DOCUMENT NUMBER: 115:256016

TITLE: Preparation of diarylstyrylquinoline diacids as  
leukotriene antagonists

INVENTOR(S): Young, Robert N.; Gauthier, Jacques Yves; Zamboni,  
Robert; Belley, Michel L.

PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Cote d'Ivoire

SOURCE: Eur. Pat. Appl., 144 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

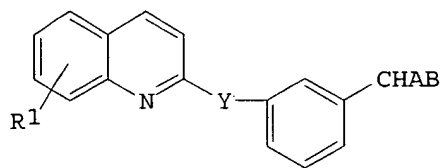
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 399818	A1	19901128	EP 1990-305640	19900523 <--
EP 399818	B1	19950816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5104882	A	19920414	US 1990-527236	19900522 <--
CA 2017376	AA	19901124	CA 1990-2017376	19900523 <--
CA 2017376	C	20000718		
NO 9002301	A	19901126	NO 1990-2301	19900523 <--
AU 9055811	A1	19901213	AU 1990-55811	19900523 <--
ZA 9003983	A	19910327	ZA 1990-3983	19900523 <--
JP 03072459	A2	19910327	JP 1990-132754	19900524 <--
JP 07103107	B4	19951108		
US 5204358	A	19930420	US 1992-818598	19920109 <--
PRIORITY APPLN. INFO.:				
			US 1989-356478	A 19890524
			US 1987-125050	B2 19871125
			US 1988-275160	B2 19881122
			US 1990-527236	A3 19900522

OTHER SOURCE(S): MARPAT 115:256016  
GI



AB Title compds. I [R1 = 7-Cl, 7-MeO, 6-F3C, 7-F3C, 6-MeSO2, H, 6,7-Cl2; Y = CH:CH, CH2CH2, CH2O, CHMeCH2; A = HO2C(CH2)2S, Me2NCO(CH2)2S, 3-(HO2C)C6H4S, Me3CNHCO(CH2)2S, 4-carboxy-2-pyridyl, [(1-adamantylamino)carbonyl]ethylthio, 1-tetrazol-5-ylmethylthio, etc.; B = 2-(HO2C)C6H4CH2CH2, 3-(HO2C)C6H4, 5-carboxy-2-thiophenyl, HO2CCH2CHMe(CH2)2, 6-carboxy-2-pyridyl, 2-(Me3CNHCO)C6H4S,

3-[(1-tetrazol-5-yl)methyl]phenyl, etc.] and their salts, useful as inhibitors of leukotriene biosynthesis, antiasthmatic, antiallergic, antiinflammatory, and cytoprotective agents (no data, assays described), are prepared I may also be used to treat erosive gastritis, **inflammatory bowel** disease, prevention of SRA-release (no data). To a suspension of [(7-chloroquinolin-2-yl)methyl]triphenylphosphonium bromide in THF was added BuLi, the reaction mixture was stirred at -78° and Me 2-[3-[2-(methoxycarbonyl)ethylthio]-3-(3-formylphenyl)propyl]benzoate [preparation from 3-(BrCH<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>CN given] added, the mixture warmed to room temperature to give I

[R1

= 7-Cl; Y = CH:CH; A = HO<sub>2</sub>C(CH<sub>2</sub>)<sub>2</sub>S; B = 2-(HO<sub>2</sub>C)C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CH<sub>2</sub>] (II) as the di-Me ester, which in THF and MeOH was saponified to give II.2Na salt. A capsule, injectable suspension and tablet formulations comprising I are given. Pharmaceutical composition of I may comprise an addnl. active ingredient such as nonsteroidal antiinflammatory drug, peripheral analgesic, cyclooxygenase inhibitor, etc.

IC ICM C07D215-18

ICS C07D215-14; C07D215-20; C07D215-36; C07D401-12; C07D405-12;  
C07D409-10; A61K031-47

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1, 63

IT 9015-82-1, **Angiotensin-converting** enzyme 39391-18-9,

Cyclooxygenase 61276-89-9, Thromboxane synthetase

RL: USES (Uses)

(inhibitors, leukotriene antagonists containing)

L67 ANSWER 44 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:542275 HCAPLUS

DOCUMENT NUMBER: 115:142275

TITLE: Pharmaceutical compositions containing an  
**angiotensin-converting** enzyme (**ACE**) inhibitor for the treatment of  
hypermotility diseases of the bowel.

INVENTOR(S): Moore, Luana R. C.

PATENT ASSIGNEE(S): E. R. Squibb and Sons, Inc., USA

SOURCE: Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 418582	A2	19910327	EP 1990-116153	19900823 <--
EP 418582	A3	19921007		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2021408	AA	19910301	CA 1990-2021408	19900718 <--
JP 03093720	A2	19910418	JP 1990-222329	19900822 <--

PRIORITY APPLN. INFO.: US 1989-401377 A 19890831

AB Hypermotility diseases of the bowel (irritable bowel syndrome, etc.) are treated with an **ACE inhibitor** (e.g. captopril, fosinopril, ceramapril, enalapril, lisinopril, zofenopril) which may be administered by suppository, enema, or by oral dosage forms that release drug in the colon. Suppository and other formulations are given.

IC ICM A61K031-40

ICS A61K031-675

CC 63-6 (Pharmaceuticals)

- ST **angiotensin converting enzyme inhibitor**  
bowel hypermotility; suppository **ACE inhibitor** bowel  
hypermotility; enalapril bowel hypermotility; captopril bowel  
hypermotility; zofenopril bowel hypermotility; lisinopril bowel  
hypermotility; fosinopril bowel hypermotility; ceranapril bowel  
hypermotility
- IT Intestine, disease or disorder  
(hypermotility, treatment of, **angiotensin-converting  
enzyme inhibitors** for)
- IT Amino acids, biological studies  
RL: BIOL (Biological study)  
(phosphonate-substituted, as **angiotensin-converting  
enzyme inhibitors**, for bowel hypermotility disease treatment)
- IT Intestine, disease or disorder  
(Crohn's, treatment of, **angiotensin-converting  
enzyme inhibitor** for)
- IT **Diarrhea**  
(**chronic**, treatment of, **angiotensin-  
converting enzyme inhibitor** for)
- IT Intestine, disease or disorder  
(colitis, treatment of, **angiotensin-converting  
enzyme inhibitor** for)
- IT Peptides, biological studies  
RL: BIOL (Biological study)  
(di-, carboxyalkyl, as **angiotensin-converting  
enzyme inhibitors**, for bowel hypermotility disease treatment)
- IT Digestive tract  
(disease, diabetic, treatment of, **angiotensin-  
converting enzyme inhibitor** for)
- IT Digestion, biological  
(disorder, hypermotility, treatment of, of bowel, **angiotensin  
-converting enzyme inhibitors** for)
- IT Pharmaceutical dosage forms  
(enemas, of **angiotensin-converting enzyme  
inhibitor** for bowel hypermotility disease treatment)
- IT Carboxylic acids, biological studies  
RL: BIOL (Biological study)  
(imino, phosphonate-substituted, as **angiotensin-  
converting enzyme inhibitors**, for bowel hypermotility  
disease treatment)
- IT Intestine, disease or disorder  
(irritable bowel syndrome, treatment of, **angiotensin-  
converting enzyme inhibitor** for)
- IT Peptides, biological studies  
RL: BIOL (Biological study)  
(phosphino-, as **angiotensin-converting enzyme  
inhibitors**, for bowel hypermotility disease treatment)
- IT Pharmaceutical dosage forms  
(suppositories, of **angiotensin-converting enzyme  
inhibitor** for bowel hypermotility disease treatment)
- IT 147-85-3D, Proline, derivs.  
RL: BIOL (Biological study)  
(**angiotensin-converting enzyme inhibitors**  
, for bowel hypermotility disease treatment)
- IT 62571-86-2, Captopril 75847-73-3 76547-98-3,  
Lisinopril 81872-10-8, Zofenopril 98048-97-6, Fosinopril  
111223-26-8  
RL: BIOL (Biological study)  
(as **angiotensin-converting enzyme inhibitor**

for bowel hypermotility disease treatment)  
IT 9015-82-1, **Angiotensin-converting enzyme**  
RL: BIOL (Biological study)  
(**inhibitors of**, for bowel hypermotility disease treatment)

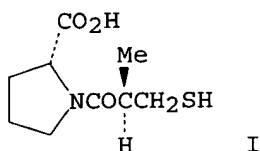
L67 ANSWER 45 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1988:161253 HCAPLUS  
DOCUMENT NUMBER: 108:161253  
TITLE: Effect of kininotropic drugs on ulcerogenesis in rats  
AUTHOR(S): Faermark, I. F.; Shvarts, G. Ya.  
CORPORATE SOURCE: VNIKhFI, Moscow, USSR  
SOURCE: Farmakologiya i Toksikologiya (Moscow) (1988  
) , 51(2), 82-4  
CODEN: FATOAO; ISSN: 0014-8318  
DOCUMENT TYPE: Journal  
LANGUAGE: Russian  
AB The effects of several kininotropic drugs on gastric ulcer development were studied in rats given ulcerogenic doses of histamine, EtOH, reserpine, and Na diclofenac. Antiulcer activities of the kininogenesis inhibitor trasylol and activator cellulose sulfate, the kinin antagonist parmidine, and the kininase inhibitors D-penicillamine and captopril were evaluated. All ulcer models responded pos. to treatments except the ulcers induced by histamine. All kininotropic drugs (except trasylol) had some degree of antiulcer activity, with parmidine being the most effective. The authors suppose that this activity is related to the effects on prostaglandin biosynthesis in the gastric mucosa.  
CC 1-9 (Pharmacology)  
ST histamine **stomach ulcer** kininotropic drug; ethanol  
**stomach ulcer** kininotropic drug; reserpine  
**stomach ulcer** kininotropic drug; diclofenac  
**stomach ulcer** kininotropic drug; trasylol  
**stomach ulcer** therapy; cellulose sulfate **stomach ulcer** therapy; parmidine **stomach ulcer** therapy; penicillamine **stomach ulcer** therapy; captopril **stomach ulcer** therapy  
IT 50-55-5, Reserpine 51-45-6, Histamine, biological studies 64-17-5, Ethanol, biological studies 15307-79-6, Sodium diclofenac  
RL: BIOL (Biological study)  
(**stomach ulcer** induced by, kininotropic drug effects on)  
IT 52-67-5, D-Penicillamine 1882-26-4, Parmidine 9032-43-3, Cellulose sulfate 62571-86-2, Captopril  
RL: BIOL (Biological study)  
(**stomach ulcer** inhibition by)  
IT 9087-70-1, Trasylol  
RL: BIOL (Biological study)  
(**stomach ulcer** response to)

L67 ANSWER 46 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 1982:400488 HCAPLUS  
DOCUMENT NUMBER: 97:488  
TITLE: Toxicological studies of captopril, an **inhibitor of angiotensin converting enzyme**. 2. One month studies on the subacute toxicity of captopril in rats  
AUTHOR(S): Imai, Kiyoshi; Yoshimura, Shinsuke; Ohtaki, Tsuneo; Hashimoto, Koroku  
CORPORATE SOURCE: Food Drug Saf. Cent., Hatano Res. Inst., Kanagawa, 257, Japan



SOURCE: Journal of Toxicological Sciences (1981),  
6(Suppl. 2), 189-214  
CODEN: JTSCDR; ISSN: 0388-1350

DOCUMENT TYPE: Journal  
LANGUAGE: Japanese  
GI



AB captopril (I) [62571-86-2] orally at 2700 mg/kg/day for 1 mo caused death in 13 of 18 male and 17 of 18 female rats, whereas I at 900 mg/kg/day caused death in 1 of 18 male and 3 of 18 female rats. Dead animals showed marked gastrointestinal tract dilation with multiple hemorrhagic erosions and/or **ulcers** in the glandular **stomach**. Animals receiving 300 mg/kg/day survived but showed polydipsia and polyuria. Animals receiving 10 or 30 mg/kg/day showed no toxicity. Blood urea-N and creatinine were elevated in rats receiving  $\geq 100$  mg/kg/day and erythrocyte counts, Hb contents, and hematocrit values were decreased in animals receiving  $\geq 300$  mg/kg/day. Afferent arterioles and interlobular arteries in the kidneys were thickened in animals receiving  $\geq 100$  mg/kg/day. Extramedullary hematopoiesis and hemosiderosis increased in the spleen and erythropoietic elements increased in the bone marrow of rats receiving  $\geq 100$  mg/kg/day. The maximum nontoxic oral dose of I was estimated to be .apprx.30 mg/kg/day in rats.

CC 1-8 (Pharmacology)

IT 62571-86-2

RL: PRP (Properties)  
(toxicity of, sex in relation to)

L67 ANSWER 47 OF 72 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1982:400487 HCAPLUS

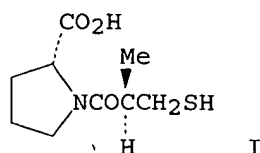
DOCUMENT NUMBER: 97:487

TITLE: Toxicological studies of captopril, an  
**inhibitor of angiotensin**  
**converting** enzyme. 1. Acute toxicological  
studies of captopril in rats and mice

AUTHOR(S): Imai, Kiyoshi; Hayashi, Yuzo; Hashimoto, Koroku  
CORPORATE SOURCE: Food Drug Saf. Cent., Hatano Res. Inst., Kanagawa,  
257, Japan

SOURCE: Journal of Toxicological Sciences (1981),  
6(Suppl. 2), 179-88  
CODEN: JTSCDR; ISSN: 0388-1350

DOCUMENT TYPE: Journal  
LANGUAGE: Japanese  
GI



AB Oral administration of captopril (I) [62571-86-2] caused decreased spontaneous motor activity, lacrimation, salivation, and a decline in body temperature in rats and mice. The LD50 values in male mice, female mice, male rats, and female rats were 4249, 5050, 4336, and 4245 mg/kg, resp. Dead animals had hemorrhagic erosion or **ulcers** in the glandular **stomach**. An i.v. I caused death by dyspnea in some mice within 3 min and delayed death in other animals. The i.p. LD50 values in male and female mice were 3154 and 3225 mg/kg, resp. Mice of both sexes tolerated s.c. I. However, at s.c. injection site necrosis was observed in the skin of rats and mice given 1600 and 1200 I/kg, resp.

CC 1-8 (Pharmacology)

IT 62571-86-2

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (toxicity of)

L67 ANSWER 48 OF 72 MEDLINE on STN

ACCESSION NUMBER: 2004307576 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15208873

TITLE: [Prophylactic use of angiotensin-converting enzyme inhibitors in indomethacin-induced ulcer and erosion lesions of the stomach].

Profilakticheskoe primeneniye ingibitorov angiotenzinprevrashchaiushchego fermenta pri iazvenno-erozivnom porazhenii zheludka, vyzhyvaemom indometatsinom.

AUTHOR: Iakubov A V; Usmanova Sh E

SOURCE: Likars'ka sprava / Ministerstvo okhorony zdorov'ia Ukrainy, (2004 Mar) (2) 47-9.

Journal code: 9601540. ISSN: 1019-5297.

PUB. COUNTRY: Ukraine

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Russian

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200411

ENTRY DATE: Entered STN: 20040624

Last Updated on STN: 20041110

Entered Medline: 20041109

AB 75% of patients systematically taking over the period of 6 weeks nonsteroidal anti-inflammatory drugs have their mucous of gastrointestinal tract pathologically changed. This process is called induced NSAID gastropathy. Inhibitors of angiotensin converting enzyme (I-ACE) seems to have gastroprotective effect by enhancing level of endogenous prostaglandins. Besides, an application of I-ACE reduces angiotensin II formation and activates renin-kallicrein-kinin system resulting in nitrogen oxide formation that is in its turn an important component of reparative process of mucous of gastrointestinal tract.

CT Check Tags: Male

Angiotensin-Converting Enzyme Inhibitors: AD, administration & dosage

\*Angiotensin-Converting Enzyme Inhibitors: TU, therapeutic use Animals

Anti-Inflammatory Agents, Non-Steroidal: TU, therapeutic use  
 \*Anti-Inflammatory Agents, Non-Steroidal: TO, toxicity  
 Arthritis, Rheumatoid: DT, drug therapy

**Captopril: AD, administration & dosage**

**Captopril: TU, therapeutic use**

Disease Models, Animal

**Enalapril: AD, administration & dosage**

**Enalapril: TU, therapeutic use**

English Abstract

Gastric Mucosa: DE, drug effects

Gastric Mucosa: PA, pathology

Indomethacin: TU, therapeutic use

\*Indomethacin: TO, toxicity

**Lisinopril: AD, administration & dosage**

**Lisinopril: TU, therapeutic use**

Rats

**Stomach Ulcer: CI, chemically induced**

**Stomach Ulcer: PA, pathology**

**\*Stomach Ulcer: PC, prevention & control**

Treatment Outcome

RN 53-86-1 (Indomethacin); 62571-86-2 (Captopril); 75847-73-3

(Enalapril); 83915-83-7 (Lisinopril)

CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Anti-Inflammatory Agents, Non-Steroidal)

L67 ANSWER 49 OF 72 MEDLINE on STN

ACCESSION NUMBER: 2004031786 MEDLINE

DOCUMENT NUMBER: PubMed ID: 14732918

TITLE: [Focal segmental glomerulosclerosis with IgA deposits in a patient with **ulcerative colitis**].  
 Glomerulosclerosi focale segmentale con depositi di IgA in un paziente con rettocolite ulcerosa.

AUTHOR: Fofi C; Nicoletti M C D; Onetti Muda A; Giulio S

CORPORATE SOURCE: U.O. Nefrologia e Dialisi, A.O.S. Camillo-Forlanini, Roma, Italy.. clafofi@tiscali.it

SOURCE: Giornale italiano di nefrologia : organo ufficiale della Societa italiana di nefrologia, (2003 Nov-Dec) 20 (6) 641-4.

Journal code: 9426434. ISSN: 0393-5590.

PUB. COUNTRY: Italy

DOCUMENT TYPE: (CASE REPORTS)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Italian

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200406

ENTRY DATE: Entered STN: 20040121

Last Updated on STN: 20040602

Entered Medline: 20040601

AB BACKGROUND: Glomerular diseases are described in patients with active **ulcerative colitis** (UC). Likely drug-induced interstitial nephritis, and nephrotic syndrome due to minimal change disease, have been reported in a few patients with UC on treatment with mesalazine and sulfasalazine (5-ASA). We describe a 33 year-old patient with a 5-years history of UC who recently developed nephrotic syndrome associated with microscopic haematuria. Blood pressure and renal function were normal. The patient was on azathioprine (AZA), mesalazine and sulfasalazine during the last year for his colitis, with good control of bowel disease. Renal biopsy revealed a focal segmental glomerulosclerosis (FSGS) associated with mesangial IgA deposits; no signs of interstitial

nephritis were found. 5-ASA was discontinued, AZA was reduced and a rapid remission of the nephrotic syndrome was observed after 6 weeks of steroid therapy (1 mg/kg/day per os) associated with ramipril 5 mg/day, with a follow-up of 9 months. CONCLUSIONS: To our knowledge this is the first report of UC and GSFS associated with IgA deposits. The occurrence of nephrotic syndrome during UC is suggestive of an association between UC and FSGS, but a possible role of mesalazine and /or sulfasalazine in its pathogenesis cannot be excluded. Mesangial IgA deposits could be an "occasional" further occurrence, considering the chronic inflammation of colonic mucosa and the altered immune response of patients with UC.

CT Check Tags: Male  
Adult  
English Abstract  
\*Glomerulosclerosis, Focal: CO, complications  
Humans  
Immunoglobulin A  
\*Proctocolitis: CO, complications  
CN 0 (Immunoglobulin A)

L67 ANSWER 50 OF 72 MEDLINE on STN  
ACCESSION NUMBER: 2003372024 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12907340  
TITLE: Colonic **ulcers** accompanying collagenous  
colitis: implication of nonsteroidal  
anti-inflammatory drugs.  
AUTHOR: Kakar Sanjay; Pardi Darrell S; Burgart Lawrence J  
CORPORATE SOURCE: Department of Pathology, Mayo Clinic, Rochester, Minnesota  
55905, USA.  
SOURCE: American journal of gastroenterology, (2003 Aug)  
98 (8) 1834-7.  
Journal code: 0421030. ISSN: 0002-9270.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200309  
ENTRY DATE: Entered STN: 20030809  
Last Updated on STN: 20030930  
Entered Medline: 20030929

AB OBJECTIVES: A small minority of otherwise typical collagenous colitis (CC) patients also have mucosal ulceration (CC-U). We studied the association of CC-U cases with ingestion of nonsteroidal anti-inflammatory drugs (NSAIDs) as a possible explanation for the mucosal ulceration. METHODS: Clinical information and histological features were reviewed in nine cases of biopsy-diagnosed CC-U. Biopsies from 18 unselected cases of CC without ulceration were reviewed for comparison. RESULTS: Of nine patients with CC-U, seven (77.8%) had a history of NSAID ingestion, compared with four of 18 CC controls (20.2%) ( $p = 0.006$ ). The diarrhea resolved after cessation of NSAID use in four CC-U patients, partially resolved in one patient, and persisted in one patient. The outcome was not available in one patient. Of the two CC-U patients who did not use NSAIDs, one patient was taking lisinopril (angiotensin-converting enzyme inhibitor), and the diarrhea resolved after stopping the drug; the ulceration in the second patient was thought to be ischemic in origin. CONCLUSIONS: Collagenous colitis with ulceration has a strong association with NSAID ingestion. Evaluation of medications and cessation of NSAIDs should be considered as a therapeutic option in cases of collagenous colitis with colonic ulceration.

CT Check Tags: Female; Male

Adult  
 Aged  
 Aged, 80 and over  
 \*Anti-Inflammatory Agents, Non-Steroidal: AE, adverse effects  
 \*Colitis: CO, complications  
 Colitis: DT, drug therapy  
 Colitis: PA, pathology  
 Colonoscopy  
 Humans  
 \*Intestinal Mucosa: PA, pathology  
 Middle Aged  
 \*Ulcer: CI, chemically induced  
 \*Ulcer: CO, complications  
 Ulcer: DI, diagnosis

CN 0 (Anti-Inflammatory Agents, Non-Steroidal)

L67 ANSWER 51 OF 72 MEDLINE on STN  
 ACCESSION NUMBER: 2001420500 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11468446  
 TITLE: **Enalapril**-induced eosinophilic gastroenteritis.  
 COMMENT: Comment in: J Clin Gastroenterol. 2002 Jul;35(1):105-6.  
 PubMed ID: 12080243  
 AUTHOR: Barak N; Hart J; Sitrin M D  
 CORPORATE SOURCE: University of Chicago, Chicago, Illinois, USA.  
 SOURCE: Journal of clinical gastroenterology, (2001 Aug)  
 33 (2) 157-8.  
 Journal code: 7910017. ISSN: 0192-0790.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: (CASE REPORTS)  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200110  
 ENTRY DATE: Entered STN: 20011008  
 Last Updated on STN: 20011008  
 Entered Medline: 20011004

AB Eosinophilic gastroenteritis is a rare disorder of unknown etiology. We describe a case of a 63-year-old woman with **chronic diarrhea** and eosinophilia. Small bowel biopsy revealed eosinophils in large clusters in the lamina propria with focal infiltration of the epithelium. The patient's diarrhea and eosinophilia started shortly after **enalapril** was prescribed. When the patient was instructed to stop taking that drug, her diarrhea promptly ceased, and the blood eosinophil level returned to normal. This is the first reported case of eosinophilic gastroenteritis associated with an angiotensin-converting enzyme inhibitor. Eosinophilic gastroenteritis should be entertained in the differential diagnosis of patients taking angiotensin-converting enzyme inhibitors who develop diarrhea or other gastrointestinal symptoms.

CT Check Tags: Female  
 Biopsy  
 Diagnosis, Differential  
 Diarrhea: ET, etiology  
**Enalapril: AD, administration & dosage**  
**\*Enalapril: AE, adverse effects**  
 \*Eosinophilia: CI, chemically induced  
 Eosinophilia: DI, diagnosis  
 Eosinophilia: PA, pathology  
 \*Gastroenteritis: CI, chemically induced

Gastroenteritis: DI, diagnosis  
 Gastroenteritis: PA, pathology  
 Humans  
 \*Hypertension: DT, drug therapy  
 Intestinal Mucosa: DE, drug effects  
 Intestinal Mucosa: PA, pathology  
 Middle Aged

RN 75847-73-3 (Enalapril)

L67 ANSWER 52 OF 72 MEDLINE on STN  
 ACCESSION NUMBER: 2000205446 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 10741273  
 TITLE: The relationship between angiogenesis and the immune response in carcinogenesis and the progression of malignant disease.  
 AUTHOR: O'Byrne K J; Dalglish A G; Browning M J; Steward W P; Harris A L  
 CORPORATE SOURCE: University Department of Oncology, Leicester Royal Infirmary, UK.. kobyne@lri.org.uk  
 SOURCE: European journal of cancer (Oxford, England : 1990), (2000 Jan) 36 (2) 151-69. Ref: 263  
 Journal code: 9005373. ISSN: 0959-8049.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200004  
 ENTRY DATE: Entered STN: 20000413  
 Last Updated on STN: 20000413  
 Entered Medline: 20000407

AB Recent studies have demonstrated that angiogenesis and suppressed cell-mediated immunity (CMI) play a central role in the pathogenesis of malignant disease facilitating tumour growth, invasion and metastasis. In the majority of tumours, the malignant process is preceded by a pathological condition or exposure to an irritant which itself is associated with the induction of angiogenesis and/or suppressed CMI. These include: cigarette smoking, chronic bronchitis and lung cancer; chronic oesophagitis and oesophageal cancer; chronic viral infections such as human papilloma virus and ano-genital cancers, chronic hepatitis B and C and hepatocellular carcinoma, and Epstein-Barr virus (EBV) and lymphomas; chronic inflammatory conditions such as Crohn's disease and **ulcerative colitis** and colorectal cancer; asbestos exposure and mesothelioma and excessive sunlight exposure/sunburn and malignant melanoma. Chronic exposure to growth factors (insulin-like growth factor-I in acromegaly), mutations in tumour suppressor genes (TP53 in Li Fraumeni syndrome) and long-term exposure to immunosuppressive agents (cyclosporin A) may also give rise to similar environments and are associated with the development of a range of solid tumours. The increased blood supply would facilitate the development and proliferation of an abnormal clone or clones of cells arising as the result of: (a) an inherited genetic abnormality; and/or (b) acquired somatic mutations, the latter due to local production and/or enhanced delivery of carcinogens and mutagenic growth factors. With progressive detrimental mutations and growth-induced tumour hypoxia, the transformed cell, to a lesser or greater extent, may amplify the angiogenic process and CMI suppression, thereby facilitating further tumour growth and metastasis. There is accumulating evidence that long-term treatment with cyclo-oxygenase

inhibitors (aspirin and indomethacin), cytokines such as interferon-alpha, anti-oestrogens (tamoxifen and raloxifene) and **captopril** significantly reduces the incidence of solid tumours such as breast and colorectal cancer. These agents are anti-angiogenic and, in the case of aspirin, indomethacin and interferon-alpha have proven immunomodulatory effects. Collectively these observations indicate that angiogenesis and suppressed CMI play a central role in the development and progression of malignant disease.

CT Disease Progression  
Gene Silencing  
Genes, p53: IM, immunology  
Humans  
Hygiene  
\*Neoplasms: BS, blood supply  
Neoplasms: DT, drug therapy  
Neoplasms: IM, immunology  
\*Neovascularization, Pathologic: ET, etiology  
Neovascularization, Pathologic: IM, immunology  
Prostaglandin-Endoperoxide Synthase: IM, immunology  
Receptors, Interferon: IM, immunology  
Research Support, Non-U.S. Gov't  
CN 0 (Receptors, Interferon); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

L67 ANSWER 53 OF 72 MEDLINE on STN  
ACCESSION NUMBER: 1998445718 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9772541  
TITLE: The decrease of gastric mucosal blood flow in obstructive jaundice under stress.  
AUTHOR: Yang N; Xu W; Duan J  
CORPORATE SOURCE: Department of Surgery, People's Hospital, Beijing Medical University.  
SOURCE: Zhonghua yi xue za zhi, (1997 Sep) 77 (9) 692-4.  
Journal code: 7511141. ISSN: 0376-2491.  
PUB. COUNTRY: China  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Chinese  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199811  
ENTRY DATE: Entered STN: 19990106  
Last Updated on STN: 19990106  
Entered Medline: 19981109

AB OBJECTIVE: To investigate the cause of decrease of gastric mucosal blood flow (GMBF) in obstructive jaundice under stress. METHODS: With common bile duct ligation (CBDL) in Wistar rats under cold restraint stress, GMBF and the content of Endothelin-1, Angiotensin-II, H2, alpha 1 receptor in gastric mucosa were measured. Before stress anti-ET-1 serum, **Enalapril**, Cimetidine and Phetolamins were administrated, and the change of GMBF was studied. RESULTS: GMBF was significantly decreased in CBDL in stress than those in control subjects. The content of ET1 and Ang-II was significantly increased, the density of H2 and alpha 1 receptor was significantly decreased. Before stress antagonist was administrated, and GMBF was significantly increased. CONCLUSION: GMBF was decreased by increased ET, Ang-II and decreased H2, alpha 1 receptor in CBDL, under stress. Antagonist improved gastric mucosal blood flow. They had protection from gastric mucosa.

CT Check Tags: Male  
Angiotensin II: ME, metabolism  
Animals

\*Cholestasis: PP, physiopathology  
Cold  
\*Endothelin-1: ME, metabolism  
English Abstract  
\*Gastric Mucosa: BS, blood supply  
Rats  
Rats, Wistar  
Receptors, Histamine H2: ME, metabolism  
Regional Blood Flow  
**Stomach Ulcer: PC, prevention & control**  
Stress

RN 11128-99-7 (Angiotensin II)

CN 0 (Endothelin-1); 0 (Receptors, Histamine H2)

L67 ANSWER 54 OF 72 MEDLINE on STN

ACCESSION NUMBER: 1998220075 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9559321

TITLE: The effects of **captopril** and naloxone on restraint-cold-stress- and ethanol-induced gastric lesions in rats.

AUTHOR: Uluoglu C; Guney Z; Kilinc M; Bozkurt S; Ercan Z S

CORPORATE SOURCE: Department of Pharmacology, Faculty of Medicine, Gazi University, Ankara, Turkey.

SOURCE: General pharmacology, (1998 May) 30 (5) 701-4.

Journal code: 7602417. ISSN: 0306-3623.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199805

ENTRY DATE: Entered STN: 19980529

Last Updated on STN: 19980529

Entered Medline: 19980519

AB 1. This study was undertaken to investigate the effect of **captopril** (1 microgram/kg or 1 mg/kg, i.p.) on the actions of naloxone (5 mg/kg, i.p. in gastric ulceration induced by ethanol and restraint-cold-stress. 2. Neither naloxone (5 mg/kg, i.p.) nor **captopril** (1 mg/kg, i.p.) alone induced any change in the indices of the ulcer in either group. 3. **Captopril** at a lower dose (1 microgram/kg, i.p.), when combined with naloxone (5 mg/kg, i.p.), significantly reduced cumulative ulcer length only in the ethanol-treated group (from 54.9 +/- 7.2 mm to 22.5 +/- 6.2 mm). 4. However, a high dose of **captopril** (1 mg/kg) plus naloxone pretreatment caused a significant reduction in both ethanol (from 54.9 +/- 7.2 mm to 24.9 +/- 6.5 mm) and restraint-cold-stress (from 19.0 +/- 3.0 mm to 5.3 +/- 1.0 mm)-induced ulcer formation. 5. Acetylsalicylic acid, when used together with **captopril**, increased the ulcer formation induced by stress. 6. Naloxone, by increasing the release of prostaglandins, has been shown to prevent ulcer formation induced by several noxious stimuli. 7. Therefore, the effect of the combination might be due to the synergistic interaction of both drugs on prostaglandin synthesis.

CT Check Tags: Female; Male

**Angiotensin-Converting Enzyme Inhibitors: PD, pharmacology**

**\*Angiotensin-Converting Enzyme Inhibitors: TU, therapeutic use**  
Animals

**Captopril: PD, pharmacology**

**\*Captopril: TU, therapeutic use**

Drug Synergism

Drug Therapy, Combination



Ethanol  
 Naloxone: PD, pharmacology  
 \*Naloxone: TU, therapeutic use  
 Prostaglandins: ME, metabolism  
 Rats  
 Restraint, Physical  
 \*Stomach Ulcer: DT, drug therapy  
 Stomach Ulcer: ET, etiology  
 Stress

RN 465-65-6 (Naloxone); 62571-86-2 (Captopril); 64-17-5 (Ethanol)  
 CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Prostaglandins)

L67 ANSWER 55 OF 72 MEDLINE on STN

ACCESSION NUMBER: 97162131 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9009118

TITLE: Cigarette smoke increases gastric ulcer size in part by an angiotensin II-mediated mechanism in rats.

AUTHOR: Seno K; Zhu J H; Barrett J D; Eggena P; Scremin O U; Lam K; Leung J W; Leung F W

CORPORATE SOURCE: Gastroenterology Laboratory, Sepulveda and West Los Angeles Veterans Administration Medical Center California, 91343, USA.

SOURCE: Digestive diseases and sciences, (1997 Jan) 42 (1) 74-8.

Journal code: 7902782. ISSN: 0163-2116.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199702

ENTRY DATE: Entered STN: 19970305

Last Updated on STN: 19970305

Entered Medline: 19970219

AB To assess the mechanism of the effect of cigarette smoke on ulcer disease we employed a rat model in which cigarette smoke increases the size of acetic acid-induced gastric ulcer and decreases the hyperemia at the ulcer margin. We postulate that cigarette smoke increases angiotensin II (a vasoconstrictor) in ulcer tissue. Since direct measurement of angiotensin II in small tissue samples is problematic, we compared the messenger ribonucleic acid (mRNA) for its precursors (angiotensinogen and renin) in ulcer and normal gastric tissue. We also evaluated the effect of **enalapril**, which blocks the conversion of angiotensin I to angiotensin II on ulcer size. In the ulcer tissue, cigarette smoke produced a significant increase in mRNA for angiotensinogen but not for renin. **Enalapril** decreased the size of the gastric ulcer in rats exposed to cigarette smoke. The data support the possibility that in ulcer tissue cigarette smoke stimulates an angiotensin II-mediated mechanism, which may in part be responsible for the impairment of ulcer margin hyperemia and aggravation of ulcer size.

CT Check Tags: Male

Angiotensin II: ME, metabolism

\*Angiotensin II: PH, physiology

Angiotensin-Converting Enzyme Inhibitors: PD, pharmacology

Animals

**Enalapril**: PD, pharmacology

Immunoblotting

Platelet-Derived Growth Factor: AN, analysis

RNA, Messenger: AN, analysis

Rats

Rats, Sprague-Dawley  
Renin: AN, analysis  
Research Support, Non-U.S. Gov't  
Research Support, U.S. Gov't, Non-P.H.S.  
\*Smoking: AE, adverse effects  
Somatomedins: AN, analysis

**Stomach Ulcer: CI, chemically induced**

**Stomach Ulcer: ME, metabolism**

**\*Stomach Ulcer: PA, pathology**

Transforming Growth Factor beta: AN, analysis

RN 11128-99-7 (Angiotensin II); **75847-73-3 (Enalapril)**

CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Platelet-Derived Growth Factor); 0 (RNA, Messenger); 0 (Somatomedins); 0 (Transforming Growth Factor beta); EC 3.4.23.15 (Renin)

L67 ANSWER 56 OF 72 MEDLINE on STN

ACCESSION NUMBER: 96105748 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8550131

TITLE: Effect of angiotensin converting enzyme inhibitor (**captopril**) on gastric ulcer production in pylorus ligated rats.

AUTHOR: Rao S P; Sathiamoorthy A; Sathiamoorthy S S

CORPORATE SOURCE: Department of Physiology, Kasturba Medical College, Manipal.

SOURCE: Indian journal of physiology and pharmacology, (1995 Jul) 39 (3) 296-8.

Journal code: 0374707. ISSN: 0019-5499.

PUB. COUNTRY: India

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199602

ENTRY DATE: Entered STN: 19960306

Last Updated on STN: 19960306

Entered Medline: 19960220

AB Intraperitoneal injection of Angiotensin Converting Enzyme inhibitor, **captopril**, reduced significantly ( $P < 0.001$ ), the production of gastric ulcers in pylorus-ligated albino rats, compared to the control groups, irrespective of the dose schedule--single or quadruple. In the light of evidence available in the literature, it is reasonable to hypothesise that the anti-ulcer effect of **captopril** may be mediated through prostaglandins.

CT Check Tags: Female; Male

**Angiotensin-Converting Enzyme Inhibitors: AD, administration & dosage**

**\*Angiotensin-Converting Enzyme Inhibitors: TU, therapeutic use**

Animals

Anti-Ulcer Agents: AD, administration & dosage

**\*Anti-Ulcer Agents: TU, therapeutic use**

**Captopril: AD, administration & dosage**

**\*Captopril: TU, therapeutic use**

Injections, Intraperitoneal

Pylorus: PH, physiology

Rats

Rats, Wistar

**Stomach Ulcer: PA, pathology**

**\*Stomach Ulcer: PC, prevention & control**

RN **62571-86-2 (Captopril)**

CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Anti-Ulcer Agents)

L67 ANSWER 57 OF 72 MEDLINE on STN  
 ACCESSION NUMBER: 94300666 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 8028057  
 TITLE: **Captopril** decreases stress ulceration without affecting gastric perfusion during canine hemorrhagic shock.  
 AUTHOR: Cullen J J; Ephgrave K S; Broadhurst K A; Booth B  
 CORPORATE SOURCE: Department of Surgery, VA Medical Center, Iowa City, IA 52246.  
 SOURCE: Journal of trauma, (1994 Jul) 37 (1) 43-9.  
 Journal code: 0376373. ISSN: 0022-5282.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 199408  
 ENTRY DATE: Entered STN: 19940818  
 Last Updated on STN: 19940818  
 Entered Medline: 19940811

AB The renin-angiotensin axis has recently been called the source of disproportionate splanchnic vasoconstriction during shock, and blocking this axis decreased gastric stress ulceration during swine cardiogenic shock. The present study tested whether the angiotensin converting enzyme inhibitor **captopril** would prevent stress ulceration when given after the onset of canine hemorrhagic shock, and whether any detrimental effects would result from enhancing splanchnic perfusion with **captopril** during hemorrhagic shock. We found that **captopril** treatment was associated with a decrease in gastric mucosal injury and with a marked decrease in systemic acidosis. **Captopril** enhanced blood flow to the small intestine, pancreas, liver, and spleen, but not flow to the stomach, during shock. Following the reinfusion of shed blood, the **captopril**-treated animals had decreased mean blood pressures and increased heart rates compared with untreated animals. We found **captopril** alleviated the stress ulceration produced by canine hemorrhagic shock, but concluded that the likely mechanism was alleviating systemic acidosis through enhanced perfusion of other viscera rather than a specific enhancement of gastric perfusion.

CT Analysis of Variance  
 Animals  
 \***Captopril**: TU, therapeutic use  
 Disease Models, Animal  
 Dogs  
 Gastric Mucosa: DE, drug effects  
 Regional Blood Flow: DE, drug effects  
 Regression Analysis  
 Research Support, U.S. Gov't, Non-P.H.S.  
 \*Shock, Hemorrhagic: CO, complications  
 Shock, Hemorrhagic: PP, physiopathology  
 Splanchnic Circulation: DE, drug effects  
 Stomach Ulcer: ET, etiology  
 Stomach Ulcer: PP, physiopathology  
 \*Stomach Ulcer: PC, prevention & control  
 \*Stress: CO, complications  
 Stress: PP, physiopathology  
 Treatment Outcome

RN 62571-86-2 (**Captopril**)

L67 ANSWER 58 OF 72 MEDLINE on STN  
ACCESSION NUMBER: 91139209 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2286425  
TITLE: Comparison of the effects of **captopril** and **enalapril** on oxyphenbutazone and ethanol-induced gastric lesions in rats.  
AUTHOR: D'Souza R S; Bhounsule S A; Dhume V G  
CORPORATE SOURCE: Department of Pharmacology, Goa Medical College, Bambolim.  
SOURCE: Indian journal of physiology and pharmacology, (1990 Jul) 34 (3) 206-8.  
Journal code: 0374707. ISSN: 0019-5499.  
PUB. COUNTRY: India  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199103  
ENTRY DATE: Entered STN: 19910412  
Last Updated on STN: 19980206  
Entered Medline: 19910325  
AB We have compared the effect of the converting enzyme inhibitors, **captopril** and **enalapril**, on two models of gastric ulcers, viz; ethanol and oxyphenbutazone-induced lesions in rats. Both **captopril** and **enalapril** did not affect ethanol-induced lesions. While **captopril** significantly protected against oxyphenbutazone-induced lesions, **enalapril** aggravated the lesions. This difference is probably due to the lack of the protective sulfhydryl group in the chemical structure of **enalapril**.  
CT Check Tags: Comparative Study; Male  
Animals  
\***Captopril**: PD, pharmacology  
\***Enalapril**: PD, pharmacology  
\*Ethanol  
\*Oxyphenbutazone  
Rats  
Rats, Inbred Strains  
Stomach Ulcer: CI, chemically induced  
\*Stomach Ulcer: PC, prevention & control  
RN 129-20-4 (Oxyphenbutazone); 62571-86-2 (**Captopril**); 64-17-5 (Ethanol); 75847-73-3 (**Enalapril**)

L67 ANSWER 59 OF 72 MEDLINE on STN  
ACCESSION NUMBER: 90255525 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2187703  
TITLE: Effect of **captopril** on oxyphenbutazone and ethanol-induced gastric lesions in rats.  
AUTHOR: Bhounsule S A; Pereira J S; Hede S S; Diniz D'Souza R S  
CORPORATE SOURCE: Department of Pharmacology, Goa Medical College, Bambolim, India.  
SOURCE: European journal of pharmacology, (1990 Feb 20) 177 (1-2) 87-90.  
Journal code: 1254354. ISSN: 0014-2999.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199006  
ENTRY DATE: Entered STN: 19900720  
Last Updated on STN: 19980206  
Entered Medline: 19900628

AB We studied the effect of the angiotensin converting enzyme inhibitor, **captopril**, on two models of gastric ulcers; oxyphenbutazone and ethanol-induced lesions. There was a significant protective effect against oxyphenbutazone-induced ulcers, which was prevented by prior administration of indomethacin. **Captopril**, however, failed to protect against ethanol-induced lesions. These findings are discussed in the light of **captopril** being a sulfhydryl compound with prostaglandin-releasing activity.

CT Check Tags: Male

Animals

\***Captopril**: PD, pharmacology

\*Ethanol

Indomethacin: PD, pharmacology

\*Oxyphenbutazone

Rats

Rats, Inbred Strains

**Stomach Ulcer**: CI, chemically induced

\***Stomach Ulcer**: PC, prevention & control

RN 129-20-4 (Oxyphenbutazone); 53-86-1 (Indomethacin); 62571-86-2 (**Captopril**); 64-17-5 (Ethanol)

L67 ANSWER 60 OF 72 MEDLINE on STN

ACCESSION NUMBER: 80208887 MEDLINE

DOCUMENT NUMBER: PubMed ID: 6104247

TITLE: Neurological dysfunction in two patients receiving **captopril** and cimetidine.

AUTHOR: Atkinson A B; Brown J J; Lever A F; McAreavey D; Robertson J I; Behan P O; Melville I D; Weir A I

SOURCE: Lancet, (1980 Jul 5) 2 (8184) 36-7.  
Journal code: 2985213R. ISSN: 0140-6736.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: (CASE REPORTS)

Letter

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 198008

ENTRY DATE: Entered STN: 19900315

Last Updated on STN: 20000303

Entered Medline: 19800828

CT Check Tags: Female; Male

\***Captopril**: AE, adverse effects

\*Cimetidine: AE, adverse effects

\*Guanidines: AE, adverse effects

Humans

Hypertension: DT, drug therapy

Middle Aged

\*Peripheral Nervous System Diseases: CI, chemically induced

\*Polyradiculoneuropathy: CI, chemically induced

\*Proline: AA, analogs & derivatives

**Stomach Ulcer**: DT, drug therapy

RN 147-85-3 (Proline); 51481-61-9 (Cimetidine); 62571-86-2 (**Captopril**)

CN 0 (Guanidines)

L67 ANSWER 61 OF 72 MEDLINE on STN

ACCESSION NUMBER: 79071878 MEDLINE

DOCUMENT NUMBER: PubMed ID: 82838

TITLE: Serum angiotensin-converting enzyme (SACE) in sarcoidosis and other granulomatous disorders.

AUTHOR: Studdy P; Bird R; James D G  
SOURCE: Lancet, (1978 Dec 23-30) 2 (8104-5) 1331-4.  
Journal code: 2985213R. ISSN: 0140-6736.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 197902  
ENTRY DATE: Entered STN: 19900314  
Last Updated on STN: 19980206  
Entered Medline: 19790223

AB Serum angiotensin-converting enzyme (SACE) activity was significantly higher in 90 patients with sarcoidosis (55 +/- [S.D.] 23 nmol min<sup>-1</sup> ml<sup>-1</sup>) than in 80 healthy controls (34 +/- 9 nmol min<sup>-1</sup> ml<sup>-1</sup>). Steroid therapy modified SACE activity; 60 sarcoidosis patients who were not being treated with steroids had significantly higher enzyme activities (58 +/- 24 nmol min<sup>-1</sup> ml<sup>-1</sup>) than 30 steroid-treated sarcoidosis patients (40 +/- 19 nmol min<sup>-1</sup> ml<sup>-1</sup>). In 50% of the non-steroid treated sarcoidosis patients SACE activity was more than 2 S.D. above the mean value for the controls. SACE activity was measured in 22 tuberculous patients (38 +/- 14 nmol min<sup>-1</sup> ml<sup>-1</sup>), 20 leprosy patients (34 +/- 9 nmol min<sup>-1</sup> ml<sup>-1</sup>), 31 with primary biliary cirrhosis (44 +/- 20 nmol min<sup>-1</sup> ml<sup>-1</sup>), 26 with inflammatory bowel disease (31 +/- 9 nmol min<sup>-1</sup> ml<sup>-1</sup>), 8 with hepatic granulomatous disease, 5 with Hodgkin's disease, and 2 with schistosomiasis. The combined false-positive rate for these non-sarcoidosis patients was 10%. Serial SACE assays provide useful information on the course of sarcoidosis and response to steroid treatment.

CT Check Tags: Female; Male  
Acute Disease  
Adolescent  
Adult  
Aged  
Angiotensin-Converting Enzyme Inhibitors  
Chronic Disease  
Enteritis: EN, enzymology  
Enzyme Inhibitors  
Granuloma: EN, enzymology  
Hodgkin Disease: EN, enzymology  
Humans  
Leprosy: EN, enzymology  
Liver Cirrhosis, Biliary: EN, enzymology  
Liver Diseases: EN, enzymology  
Middle Aged  
\*Peptidyl-Dipeptidase A: BL, blood  
Prednisolone: TU, therapeutic use  
Sarcoidosis: DT, drug therapy  
\*Sarcoidosis: EN, enzymology  
Schistosomiasis: EN, enzymology  
Tuberculosis, Pulmonary: EN, enzymology

RN 50-24-8 (Prednisolone)

CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Enzyme Inhibitors); EC 3.4.15.1 (Peptidyl-Dipeptidase A)

L67 ANSWER 62 OF 72 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004506805 EMBASE

TITLE: Models for evaluating agents intended for the prophylaxis, mitigation and treatment of radiation injuries report of an

NCI workshop, December 3-4, 2003.

AUTHOR: Stone H.B.; Moulder J.E.; Coleman C.N.; Ang K.K.; Anscher M.S.; Barcellos-Hoff M.H.; Dynan W.S.; Fike J.R.; Grdina D.J.; Greenberger J.S.; Hauer-Jensen M.; Hill R.P.; Kolesnick R.N.; MacVittie T.J.; Marks C.; McBride W.H.; Metting N.; Pellmar T.; Purucker M.; Robbins M.E.; Schiestl R.H.; Seed T.M.; Tomaszewski J.E.; Travis E.L.; Wallner P.E.; Wolpert M.; Zaharevitz D.

CORPORATE SOURCE: H.B. Stone, EPN 6015A, MSC 7440, 6130 Executive Blvd., Bethesda, MD 20892-7440, United States. stoneh@mail.nih.gov

SOURCE: Radiation Research, (2004) Vol. 162, No. 6, pp. 711-728.  
Refs: 199  
ISSN: 0033-7587 CODEN: RAREAE

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 014 Radiology  
016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20041230  
Last Updated on STN: 20041230

AB To develop approaches to prophylaxis/protection, mitigation and treatment of radiation injuries, appropriate models are needed that integrate the complex events that occur in the radiation-exposed organism. While the spectrum of agents in clinical use or preclinical development is limited, new research findings promise improvements in survival after whole-body irradiation and reductions in the risk of adverse effects of radiotherapy. Approaches include agents that act on the initial radiochemical events, agents that prevent or reduce progression of radiation damage, and agents that facilitate recovery from radiation injuries. While the mechanisms of action for most of the agents with known efficacy are yet to be fully determined, many seem to be operating at the tissue, organ or whole animal level as well as the cellular level. Thus research on prophylaxis/protection, mitigation and treatment of radiation injuries will require studies in whole animal models. Discovery, development and delivery of effective radiation modulators will also require collaboration among researchers in diverse fields such as radiation biology, inflammation, physiology, toxicology, immunology, tissue injury, drug development and radiation oncology. Additional investment in training more scientists in radiation biology and in the research portfolio addressing radiological and nuclear terrorism would benefit the general population in case of a radiological terrorism event or a large-scale accidental event as well as benefit patients treated with radiation.  
.COPYRG. 2004 by Radiation Research Society.

CT Medical Descriptors:  
\*radiation injury: CO, complication  
\*radiation injury: DT, drug therapy  
\*radiation injury: PC, prevention  
radiation protection  
cancer radiotherapy  
radiation dose fractionation  
radiation response  
hematologic disease: CO, complication  
hematologic disease: DT, drug therapy  
digestive system injury: CO, complication  
digestive system injury: DT, drug therapy

central nervous system disease: CO, complication  
central nervous system disease: DT, drug therapy  
lung injury: CO, complication  
lung injury: DT, drug therapy  
lung injury: PC, prevention  
kidney injury: CO, complication  
kidney injury: DT, drug therapy  
kidney injury: PC, prevention  
xerostomia: CO, complication  
xerostomia: DT, drug therapy  
xerostomia: PC, prevention  
**proctitis: CO, complication**  
**proctitis: DT, drug therapy**  
gastrointestinal hemorrhage: SI, side effect  
lung fibrosis: DT, drug therapy  
lung fibrosis: PC, prevention  
kidney disease: CO, complication  
kidney disease: DT, drug therapy  
fibrosis: CO, complication  
fibrosis: DT, drug therapy  
whole body radiation  
radiation hazard  
human  
nonhuman  
clinical trial  
conference paper  
priority journal  
Drug Descriptors:  
\*radioprotective agent: AE, adverse drug reaction  
\*radioprotective agent: CT, clinical trial  
\*radioprotective agent: AD, drug administration  
\*radioprotective agent: DO, drug dose  
\*radioprotective agent: DT, drug therapy  
\*radioprotective agent: IV, intravenous drug administration  
\*radioprotective agent: PD, pharmacology  
**dipeptidyl carboxypeptidase inhibitor: CT, clinical trial**  
**dipeptidyl carboxypeptidase inhibitor: DT, drug therapy**  
**dipeptidyl carboxypeptidase inhibitor: PD, pharmacology**  
amifostine: CT, clinical trial  
amifostine: AD, drug administration  
amifostine: DO, drug dose  
amifostine: DT, drug therapy  
amifostine: IV, intravenous drug administration  
amifostine: PD, pharmacology  
pentoxifylline: DT, drug therapy  
hemopoietic growth factor: DT, drug therapy  
Fas antigen: EC, endogenous compound  
androstenediol: DT, drug therapy  
interleukin 11: DT, drug therapy  
keratinocyte growth factor: DT, drug therapy  
**angiotensin: DT, drug therapy**  
antibiotic agent: DT, drug therapy  
salazosulfapyridine: DT, drug therapy  
octreotide: DT, drug therapy  
misoprostol: DT, drug therapy  
enema: DT, drug therapy  
sucralfate: DT, drug therapy  
short chain fatty acid: DT, drug therapy  
antioxidant: DT, drug therapy



antioxidant: PD, pharmacology  
 fibroblast growth factor: DT, drug therapy  
 fibroblast growth factor: PD, pharmacology  
 thrombomodulin: EC, endogenous compound  
 anticoagulant agent: AE, adverse drug reaction  
 anticoagulant agent: DT, drug therapy  
 manganese superoxide dismutase: DT, drug therapy  
 protein p53: EC, endogenous compound  
**angiotensin 2 receptor antagonist: DT, drug therapy**  
 dexamethasone: DT, drug therapy  
 mercaptamine: DT, drug therapy  
 transforming growth factor beta: EC, endogenous compound  
 halofuginone: DT, drug therapy  
 halofuginone: PD, pharmacology  
 primrose oil: DT, drug therapy  
 primrose oil: PD, pharmacology  
 primrose oil: TP, topical drug administration  
 unindexed drug

RN (amifostine) 20537-88-6; (pentoxifylline) 6493-05-6; (androstenediol) 28652-91-7, 521-17-5; (keratinocyte growth factor) 126469-10-1; (**angiotensin**) 11128-99-7, 1407-47-2; (salazosulfapyridine) 599-79-1; (octreotide) 83150-76-9; (misoprostol) 59122-46-2, 59122-48-4; (sucralfate) 54182-58-0; (fibroblast growth factor) 62031-54-3; (thrombomodulin) 112049-68-0; (dexamethasone) 50-02-2; (mercaptamine) 156-57-0, 60-23-1; (halofuginone) 55837-20-2, 64924-67-0, 7695-84-3; (primrose oil) 65546-85-2  
 CN Wr 2721

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ACCESSION NUMBER: 2004465928 EMBASE  
 TITLE: Diabetes mellitus and pregnancy: The GP's role.  
 AUTHOR: Cheung W.; McElduff A.  
 CORPORATE SOURCE: Dr. W. Cheung, Department of Diabetes/Endocrinology, Westmead Hospital, Sydney, NSW, Australia  
 SOURCE: Medicine Today, (2004) Vol. 5, No. 10, pp. 16-22.  
 ISSN: 1443-430X CODEN: MTNBCV  
 COUNTRY: Australia  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 003 Endocrinology  
 007 Pediatrics and Pediatric Surgery  
 010 Obstetrics and Gynecology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 20041119  
 Last Updated on STN: 20041119

AB • Pregnancy outcomes in patients With diabetes can be optimised by appropriate care. Preconception counselling and meticulous glycaemic control before and during pregnancy are essential. • Patients need assessment for the presence of micro- and macrovascular complications of diabetes. Some of these need therapy before pregnancy (e.g. retinopathy) while others increase the likelihood of problems in pregnancy (e.g. autonomic neuropathy or nephropathy) or place the mother's health at increased risk (e.g. macrovascular disease). • Postpartum counselling and adjustment of insulin therapy is required to ensure patient safety. • Drug therapy, including complementary therapy, should be reviewed.  
 CT Medical Descriptors:  
 \*maternal diabetes mellitus: DT, drug therapy

gestation period  
maternal care  
general practitioner  
patient counseling  
congenital disorder: CO, complication  
congenital disorder: CN, congenital disorder  
perinatal mortality  
hemoglobin determination  
risk assessment  
statistical analysis  
statistical significance  
macrosomia: CO, complication  
macrosomia: CN, congenital disorder  
hypoglycemia: CO, complication  
hypoglycemia: CN, congenital disorder  
preeclampsia: CO, complication  
preeclampsia: CN, congenital disorder  
drug safety  
drug contraindication  
patient education  
hypertension: DT, drug therapy  
glucose blood level  
thyroid function test  
hypothyroidism: CO, complication  
**celiac disease: CO, complication**  
practice guideline  
puerperium  
breast feeding  
human  
female  
fetus  
newborn  
adult  
review  
Drug Descriptors:  
hemoglobin Alc: EC, endogenous compound  
oral antidiabetic agent: DT, drug therapy  
oral antidiabetic agent: PO, oral drug administration  
insulin: DT, drug therapy  
metformin: DT, drug therapy  
metformin: PO, oral drug administration  
**dipeptidyl carboxypeptidase inhibitor**  
**angiotensin receptor antagonist**  
diuretic agent  
beta adrenergic receptor blocking agent  
methyldopa: DT, drug therapy  
hydralazine: DT, drug therapy  
verapamil: DT, drug therapy  
antilipemic agent  
isophane insulin: DT, drug therapy  
insulin zinc suspension: DT, drug therapy  
insulin[B28 lysine B29 proline]: DT, drug therapy  
insulin aspart: DT, drug therapy  
insulin glargine: DT, drug therapy  
thyrotropin: EC, endogenous compound  
neutral insulin: DT, drug therapy  
hypurin neutral  
hypurin isophane  
humulin 1

humulin ul  
 RN (hemoglobin A1c) 62572-11-6; (insulin) 9004-10-8; (metformin) 1115-70-4, 657-24-9; (methyldopa) 555-29-3, 555-30-6; (hydralazine) 304-20-1, 86-54-4; (verapamil) 152-11-4, 52-53-9; (isophane insulin) 9004-17-5; (insulin zinc suspension) 8049-62-5; (insulin[B28 lysine B29 proline]) 133107-64-9; (insulin aspart) 116094-23-6; (insulin glargine) 160337-95-1; (thyrotropin) 9002-71-5; (neutral insulin) 9004-14-2  
 CN Actrapid; Humulin r; Hypurin neutral; Hypurin isophane; Protaphane; Monotard; Humulin l; Ultratard; Humulin ul; Humalog; Novorapid; Lantus

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ACCESSION NUMBER: 2003483636 EMBASE  
 TITLE: Scleroderma: A treatable disease.  
 AUTHOR: Korn J.H.  
 CORPORATE SOURCE: Dr. J.H. Korn, Rheumatology Section, Boston University Medical Center, 80 East Concord Street, Boston, MA 02118, United States  
 SOURCE: Cleveland Clinic Journal of Medicine, (2003) Vol. 70, No. 11, pp. 954-968.  
 Refs: 9  
 ISSN: 0891-1150 CODEN: CCJMEL  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 013 Dermatology and Venereology  
 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
 028 Urology and Nephrology  
 031 Arthritis and Rheumatism  
 037 Drug Literature Index  
 038 Adverse Reactions Titles  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 20031211  
 Last Updated on STN: 20031211

AB Many effective treatments for scleroderma have emerged in recent years, including bosentan, an endothelin receptor antagonist, and epoprostenol, a prostacyclin, both of which target vasoconstriction. Cyclophosphamide may soon be proven effective against interstitial lung disease.

CT Medical Descriptors:  
 \*scleroderma: DI, diagnosis  
 \*scleroderma: DT, drug therapy  
 \*scleroderma: PC, prevention  
 \*scleroderma: TH, therapy  
 treatment planning  
 interstitial lung disease: CO, complication  
 interstitial lung disease: DI, diagnosis  
 interstitial lung disease: DT, drug therapy  
 vasoconstriction  
 survival rate  
 clinical feature  
 kidney disease: CO, complication  
 kidney disease: DI, diagnosis  
 kidney disease: DT, drug therapy  
 lung disease: CO, complication  
 Raynaud phenomenon: DT, drug therapy  
 Raynaud phenomenon: TH, therapy  
 vascular disease  
 blood vessel injury  
 warming

skin ulcer: DT, drug therapy  
superinfection: DT, drug therapy  
blood pressure monitoring  
urinalysis  
hypertension: DI, diagnosis  
hypertension: DT, drug therapy  
proteinuria: DI, diagnosis  
proteinuria: DT, drug therapy  
bronchiectasis: CO, complication  
aspiration pneumonia: CO, complication  
pleura disease: CO, complication  
pleura effusion: CO, complication  
fibrosing alveolitis: CO, complication  
fibrosing alveolitis: DI, diagnosis  
fibrosing alveolitis: DT, drug therapy  
computer assisted tomography  
lung function test  
lung biopsy  
pulmonary hypertension: CO, complication  
pulmonary hypertension: DT, drug therapy  
syndrome CREST  
quality of life  
skin manifestation: SI, side effect  
gastrointestinal disease: DT, drug therapy  
gastrointestinal reflux: DT, drug therapy  
    **chronic diarrhea: DT, drug therapy**  
stomach antrum vascular ectasia: SU, surgery  
laser surgery  
cardiovascular disease  
fibrosis  
human  
clinical trial  
article  
Drug Descriptors:  
bosentan: DT, drug therapy  
bosentan: PD, pharmacology  
endothelin receptor antagonist: DT, drug therapy  
endothelin receptor antagonist: PD, pharmacology  
prostacyclin: CT, clinical trial  
prostacyclin: DT, drug therapy  
prostacyclin: PD, pharmacology  
prostacyclin derivative: AE, adverse drug reaction  
prostacyclin derivative: CT, clinical trial  
prostacyclin derivative: DT, drug therapy  
prostacyclin derivative: IH, inhalational drug administration  
prostacyclin derivative: IV, intravenous drug administration  
prostacyclin derivative: SC, subcutaneous drug administration  
cyclophosphamide: DT, drug therapy  
cyclophosphamide: PD, pharmacology  
carbon monoxide  
calcium channel blocking agent: DT, drug therapy  
alpha adrenergic receptor blocking agent: DT, drug therapy  
glyceryl trinitrate: DT, drug therapy  
    **dipeptidyl carboxypeptidase inhibitor: DT, drug therapy**  
    **dipeptidyl carboxypeptidase inhibitor: PD, pharmacology**  
antibiotic agent: DT, drug therapy  
cefalexin: DT, drug therapy  
dicloxacillin: DT, drug therapy  
ciprofloxacin: DT, drug therapy

vasodilator agent: DT, drug therapy  
 vasodilator agent: IH, inhalational drug administration  
 vasodilator agent: IA, intraarterial drug administration  
 sildenafil: DT, drug therapy

**angiotensin receptor antagonist: DT, drug therapy**

creatinine: EC, endogenous compound  
 bone morphogenetic protein 2: EC, endogenous compound  
 angiopoietin 1: EC, endogenous compound  
 angiopoietin 2: EC, endogenous compound  
 anticoagulant agent: DT, drug therapy  
 uniprost: AE, adverse drug reaction  
 uniprost: DT, drug therapy  
 uniprost: SC, subcutaneous drug administration  
 nitric oxide: DT, drug therapy  
 nitric oxide: IH, inhalational drug administration  
 iloprost: DT, drug therapy  
 iloprost: IH, inhalational drug administration  
 endothelin: EC, endogenous compound  
 placebo  
 proton pump inhibitor: DT, drug therapy  
 histamine H2 receptor antagonist: DT, drug therapy  
 unindexed drug

RN (bosentan) 147536-97-8, 157212-55-0; (prostacyclin) 35121-78-9,  
 61849-14-7; (cyclophosphamide) 50-18-0; (carbon monoxide) 630-08-0;  
 (glyceryl trinitrate) 55-63-0; (cefalexin) 15686-71-2, 23325-78-2;  
 (dicloxacillin) 13412-64-1, 3116-76-5, 343-55-5; (ciprofloxacin)  
 85721-33-1; (sildenafil) 139755-83-2; (creatinine) 19230-81-0, 60-27-5;  
 (angiopoietin 1) 186270-49-5; (angiopoietin 2) 194368-66-6; (uniprost)  
 81846-19-7; (nitric oxide) 10102-43-9; (iloprost) 78919-13-8, 82889-99-4  
 CN Flolan; Viagra; Tracleer; Cytoxan; Neosar; Remodulin; Ilomedin

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ACCESSION NUMBER: 2003277210 EMBASE

TITLE: Steroid therapy reduces mesangial matrix accumulation in advanced IgA nephropathy.

AUTHOR: Kuriki M.; Asahi K.; Asano K.; Sakurai K.; Eiro M.; Suzuki H.; Watanabe K.; Katoh T.; Watanabe T.

CORPORATE SOURCE: Dr. T. Katoh, Department of Internal Medicine III, Fukushima Medical Univ. Sch. of Med., 1 Hikarigaoka, Fukushima 960-1295, Japan. t-katoh@fmu.ac.jp

SOURCE: Nephrology Dialysis Transplantation, (1 Jul 2003) Vol. 18, No. 7, pp. 1311-1315.

Refs: 16

ISSN: 0931-0509 CODEN: NDTREA

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
 028 Urology and Nephrology  
 037 Drug Literature Index  
 038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20030731

Last Updated on STN: 20030731

AB Background. Steroid therapy for IgA nephropathy (IgAN) has been reported to ameliorate the long-term prognosis of IgAN, but its mode of action has not been fully elucidated. In this study, we examined the effect of steroids on glomerular morphological changes in IgAN. Methods. We

examined 16 patients with biopsy-proven IgAN (male/female = 11/5, mean age 32.1 years) who were divided into prognosis groups according to criteria set by the Japanese Society of Nephrology. Initially, they received a loading dose of steroids, followed by a daily dose of 10-15 mg prednisolone. After 12 months, they underwent a second biopsy, and their histological and clinical features were examined. Results. Before and after therapy, systolic blood pressure, diastolic blood pressure, serum creatinine and creatinine clearance all remained unchanged. However, urinary protein excretion decreased dramatically, from  $1.6 \pm 1.7$  to  $0.4 \pm 0.2$  g/day ( $P < 0.005$ ). Furthermore, computerized imaging revealed a significant reduction of the mesangial matrix index (MMI) from  $14.5 \pm 5.2$  to  $9.5 \pm 3.6\%$  ( $P < 0.001$ ). The numbers of sclerosing glomeruli did not change. Conclusions. Steroid therapy reduces mesangial matrix accumulation and reduces urinary protein excretion in advanced IgAN.

CT Medical Descriptors:

\*immunoglobulin A nephropathy: DI, diagnosis  
 \*immunoglobulin A nephropathy: DT, drug therapy

kidney biopsy

prognosis

histopathology

clinical feature

systolic blood pressure

diastolic blood pressure

blood pressure monitoring

creatinine blood level

creatinine clearance

urinary excretion

image analysis

mesangium cell

extracellular matrix

glomerulosclerosis

disease severity

hypertension: CO, complication

hypertension: DT, drug therapy

proteinuria

infection: SI, side effect

**stomach ulcer: SI, side effect**

diabetes mellitus: SI, side effect

disease exacerbation: SI, side effect

human

male

female

clinical article

controlled study

human tissue

adult

article

priority journal

Drug Descriptors:

\*methylprednisolone: AE, adverse drug reaction

\*methylprednisolone: DO, drug dose

\*methylprednisolone: DT, drug therapy

\*methylprednisolone: PD, pharmacology

prednisolone: AE, adverse drug reaction

prednisolone: DO, drug dose

prednisolone: DT, drug therapy

prednisolone: PD, pharmacology

creatinine: EC, endogenous compound

steroid: AE, adverse drug reaction

steroid: DO, drug dose  
steroid: DT, drug therapy  
steroid: PD, pharmacology  
calcium antagonist: DT, drug therapy  
**dipeptidyl carboxypeptidase inhibitor**  
**angiotensin 2 receptor antagonist**  
dilazep: DT, drug therapy  
antithrombocytic agent: DT, drug therapy

RN (methylprednisolone) 6923-42-8, 83-43-2; (prednisolone) 50-24-8;  
(creatinine) 19230-81-0, 60-27-5; (dilazep) 20153-98-4, 35898-87-4

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ACCESSION NUMBER: 2003075271 EMBASE  
TITLE: Association between vitamin D receptor gene polymorphisms and tubular citrate handling in calcium nephrolithiasis.  
AUTHOR: Mossetti G.; Vuotto P.; Rendina D.; Numis F.G.; Viceconti R.; Giordano F.; Cioffi M.; Scopacasa F.; Nunziata V.  
CORPORATE SOURCE: V. Nunziata, Dipto. di Med. Clin. e Sperimentale, Universita Federico II, via S. Pansini, 5, 80131 Naples, Italy. nunziata@unina.it  
SOURCE: Journal of Internal Medicine, (1 Feb 2003) Vol. 253, No. 2, pp. 194-200.  
Refs: 44  
ISSN: 0954-6820 CODEN: JINMEO  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 006 Internal Medicine  
028 Urology and Nephrology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 20030227  
Last Updated on STN: 20030227

AB Objectives. Hypocitraturia is a risk factor for calcium nephrolithiasis. 1.25(OH)(2)D(3) influences renal citrate handling and enhances citraturia. The aim of this study was to evaluate the relationship between vitamin D receptor (VDR) allelic variant and urinary citrate excretion in recurrent stone formers (SF) patients. Design. Case-control study. Subjects. A total of 220 recurrent calcium oxalate SF patients and 114 healthy control (C) subjects were enrolled for this study. Subjects with urinary tract infections, hyperparathyroidism, cystinuria >70 µmol/24 h, gouty diathesis, renal tubular acidosis, renal failure, chronic diarrhoeal states, intake of thiazide diuretics, **angiotensin**-converting enzyme (ACE)-inhibitors, glucocorticoids or oestrogens were excluded. A standard constant diet was given for 7 days. The 24-h urinary citrate excretion and the active tubular reabsorption of filtered citrate (Rcit) were evaluated. Hypocitraturia was defined as a urinary citrate excretion lower than 1.7 mmol day<sup>-1</sup>. Stone formers patients and C were genotyped for BsmI and TaqI VDR alleles. Contingency table chi-square tests were used to compare genotype frequencies in hypocitraturic SF patients, normocitraturic SF and C. Results. The prevalence of hypocitraturia in SF patients was 32.7% (72 of 200). Hypocitraturia in these patients resulted from excessive Rcit of a normal load of citrate. We found a different distribution (P < 0.05) of BsmI and TaqI VDR genotypes in hypocitraturic SF patients compared with normocitraturic SF and C. In particular, the prevalence of bb and TT VDR genotypes in hypocitraturic SF was significantly higher than in normocitraturic SF and C. Conclusions. These results point to a genetic association between BsmI and TaqI VDR polymorphisms and idiopathic hypocitraturia in calcium-oxalate recurrent

SF patients.  
 CT Medical Descriptors:  
 \*nephrolithiasis  
 DNA polymorphism  
 risk factor  
 urine level  
 allele  
 urinary tract infection  
 hyperparathyroidism  
 cystinuria  
 gout  
 kidney tubule acidosis  
 kidney failure  
   **chronic diarrhea**  
 standard  
 diet  
 kidney tubule absorption  
 genotype  
 chi square test  
 prevalence  
 genetic association  
 disease association  
 case control study  
 human  
 male  
 female  
 major clinical study  
 controlled study  
 adult  
 article  
 priority journal  
 Drug Descriptors:  
 \*vitamin D receptor: EC, endogenous compound  
 \*citric acid: EC, endogenous compound  
 \*calcium: EC, endogenous compound  
 thiazide diuretic agent  
   **dipeptidyl carboxypeptidase inhibitor**  
 glucocorticoid  
 estrogen  
 calcium oxalate: EC, endogenous compound  
 RN (citric acid) 126-44-3, 5949-29-1, 77-92-9, 8002-14-0; (calcium)  
 7440-70-2; (calcium oxalate) 563-72-4  
  
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 reserved on STN  
 ACCESSION NUMBER: 2002194944 EMBASE  
 TITLE: [Unrecognized causes of chronic cough].  
 CAUSES MECONNUES DE TOUX CHRONIQUE.  
 AUTHOR: Auliac J.B.; Bota S.; Nouvet G.  
 CORPORATE SOURCE: G. Nouvet, Clinique Pneumologique, CHRU de Rouen, Hopital C  
 Nicolle, 1 rue de Germont, 76031 Rouen Cedex, France.  
 georges.nouvet@chu-rouen.fr  
 SOURCE: Revue des Maladies Respiratoires, (2002) Vol. 19, No. 2 I,  
 pp. 207-216.  
 Refs: 81  
 ISSN: 0761-8425 CODEN: RMREEY  
 COUNTRY: France  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis



037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: French  
SUMMARY LANGUAGE: English; French  
ENTRY DATE: Entered STN: 20020620  
Last Updated on STN: 20020620

AB Chronic cough is defined as persistence of the symptom for longer than one month. It is a common reason for consultation. A systematic diagnostic approach based on the history, clinical examination and a number of investigations (chest x-ray, lung function tests, oesophageal pH monitoring and sinus x-rays) reveals the cause in most cases. The main aetiologies are post-nasal drip, gastro-oesophageal reflux, asthma, chronic bronchitis, and the use of angiotensin converting enzyme inhibitors. Nevertheless, in some cases, the cause is not found. In this situation it is necessary to search for less common pathologies where cough is just a symptom of systemic disease, such as connective tissue disorder (Sjogren's syndrome, atrophic polychondritis), vasculitis (Wegener's granulomatosis), Horton's syndrome (cluster headaches), amyloidosis and inflammatory bowel disease. It may also be a matter of local pathology of the tracheo-bronchial tree, such as tracheo-bronchomegaly, tracheopathia osteoplastica, rare or unrecognized infections (whooping cough, post-viral cough, bronchial tuberculosis), reactive bronchial dysfunction, eosinophilic bronchitis or radiologically occult bronchial carcinoma. It is also necessary to consider vocal cord dysfunction and cough due to medication before accepting a diagnosis of psychogenic cough.

CT Medical Descriptors:

\*coughing: ET, etiology  
\*coughing: SI, side effect  
chronic disease: ET, etiology  
chronic disease: SI, side effect  
symptom  
diagnostic approach route  
anamnesis  
clinical examination  
diagnostic imaging  
thorax radiography  
lung function test  
esophagus pH  
pH measurement  
gastroesophageal reflux  
asthma  
chronic bronchitis  
drug use  
connective tissue disease  
Sjogren syndrome  
relapsing polychondritis  
Wegener granulomatosis  
temporal arteritis  
vasculitis  
amyloidosis  
cluster headache  
differential diagnosis  
tracheobronchial tree  
respiratory tract disease  
respiratory tract infection  
lung carcinoma  
vocal cord paralysis  
idiopathic disease

gastrointestinal disease  
human  
review

Drug Descriptors:

**dipeptidyl carboxypeptidase inhibitor: AE, adverse drug reaction**

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ACCESSION NUMBER: 2001058753 EMBASE

TITLE: Characterization and clinical course of patients not receiving aspirin for acute myocardial infarction: Results from the MITRA and MIR studies.

AUTHOR: Frilling B.; Schiele R.; Gitt A.K.; Zahn R.; Schneider S.; Glunz H.-G.; Gieseler U.; Baumgartel B.; Asbeck F.; Senges J.

CORPORATE SOURCE: B. Frilling, Department of Cardiology, Bremserstr 79, 67063 Ludwigshafen, Germany. Frilling@klilu.de

SOURCE: American Heart Journal, (2001) Vol. 141, No. 2, pp. 200-205.

Refs: 17

ISSN: 0002-8703 CODEN: AHJOA2

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20010223

Last Updated on STN: 20010223

AB Background: Clinical trials have shown the efficacy of aspirin for acute myocardial infarction (AMI). However, not all patients receive aspirin for AMI. The aim of this study was to provide information on characteristics and clinical course of patients not treated with aspirin for AMI. Methods: We analyzed the data of the Myocardial Infarction Registry (MIR) and the Maximal Individual Therapy of Acute Myocardial Infarction (MITRA) registry. MITRA and MIR were prospective multicenter registries of patients with ST segment elevation myocardial infarction in Germany. Results: of 22,572 patients registered from 1994 to 1998, 1767 (7.8%) did not receive aspirin within the first 48 hours after admission. Multivariate analysis revealed two main factors associated with withholding aspirin for AMI: relative contraindications to aspirin (gastric ulcer [odds ratio (OR) 4.9, 95% confidence interval (CI) 3.7-5.7], renal insufficiency [OR 1.4, 95% CI 1.1-1.8]), and critical clinical state at admission (cardiogenic shock [OR 1.5, 95% CI 1.2-2.1] and prehospital resuscitation [OR 1.8, 95% CI 1.4-2.2]). In addition, these patients were significantly less likely to receive reperfusion therapy and adjunctive medical therapy such as  $\beta$ -blockers and angiotensin-converting enzyme inhibitors. In-hospital mortality after adjustment for baseline characteristics was 27.2% in patients without aspirin compared with 11.1% in patients treated with aspirin. Conclusions: Only a minority of AMI patients (7.8%) did not receive aspirin. Relative contraindications to aspirin and a critical clinical state at admission were the main factors associated with withholding aspirin for AMI. Even after adjustment for patient characteristics, the mortality of patients without aspirin was almost three times higher.

CT Medical Descriptors:

\*heart infarction: DT, drug therapy  
disease course  
mortality

drug contraindication

stomach ulcer

kidney failure

patient coding

human

male

female

major clinical study

clinical trial

aged

adult

article

priority journal

Drug Descriptors:

\*acetylsalicylic acid: CT, clinical trial

\*acetylsalicylic acid: DT, drug therapy

beta adrenergic receptor blocking agent: DT, drug therapy

**dipeptidyl carboxypeptidase inhibitor: DT, drug therapy**

tissue plasminogen activator: DT, drug therapy

streptokinase: DT, drug therapy

RN (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6,  
63781-77-1; (tissue plasminogen activator) 105913-11-9; (streptokinase)  
9002-01-1

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ACCESSION NUMBER: 1999023645 EMBASE

TITLE: Prostaglandin mediated gastric acid secretion inhibitory effect as a possible mechanism for the antiulcer effect of **angiotensin** converting enzyme inhibitor (**captopril**) in pylorus ligated rats.

AUTHOR: Rao S.P.; Murthy K.D.; Nayak B.S.; Sathiamoorthy S.S.

CORPORATE SOURCE: S.P. Rao, Department of Physiology, International Centre for Health Sci., Kasturba Medical College, Manipal - 576 119, India

SOURCE: Indian Journal of Pharmacology, (1998) Vol. 30, No. 6, pp. 385-389.

Refs: 29

ISSN: 0253-7613 CODEN: INJPD2

COUNTRY: India

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 037 Drug Literature Index

048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 19990204

Last Updated on STN: 19990204

AB Objective: To study the gastric secretory changes induced by antiulcer property of **captopril** and the role of prostaglandins in them.  
Methods: The effect of single dose of **captopril** and famotidine on different gastric parameters like ulcer index, pH, total acidity, mucopolysaccharide content and surface tension of gastric juice was studied by pyloric ligation alone and after pretreatment with ibuprofen.  
Results: **Captopril** and famotidine caused significant reduction in ulcer index and gastric acid secretion ( $p < 0.01$ ) when compared to saline control group. Both of them did not show any effect on mucus content and surface tension of gastric juice. Concurrent administration of ibuprofen reduced the anti-ulcer effect of **captopril** significantly ( $P < 0.01$ ) and nullified the acid secretion inhibitory effect of

**captopril**. However, the anti-ulcer and acid secretion inhibitory effects of famotidine were not altered by pretreatment with ibuprofen. Conclusion: **Captopril** may act through prostaglandins to inhibit gastric acid secretion and this effect of **captopril** on acid secretion may be the mechanism involved in its anti-ulcer effect.

## CT Medical Descriptors:

\***stomach ulcer: DT, drug therapy**

\*stomach acid secretion

\*pylorus ligation

prostaglandin metabolism

surface tension

stomach juice

drug effect

enzyme inhibition

stomach mucosa

stomach epithelium

stomach parietal cell

nonhuman

rat

animal experiment

animal model

controlled study

article

## Drug Descriptors:

\***captopril: DT, drug therapy**

\***captopril: PD, pharmacology**

\*famotidine: DT, drug therapy

\*famotidine: PD, pharmacology

ibuprofen

**dipeptidyl carboxypeptidase inhibitor**

RN (**captopril**) 62571-86-2; (famotidine) 76824-35-6;  
(ibuprofen) 15687-27-1

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ACCESSION NUMBER: 97145493 EMBASE

DOCUMENT NUMBER: 1997145493

TITLE: Reliability of drug utilization evaluation as an assessment of medication appropriateness.

AUTHOR: Shelton P.S.; Hanlon J.T.; Landsman P.B.; Scott M.A.; Lewis I.K.; Schmader K.E.; Samsa G.P.; Weinberger M.

CORPORATE SOURCE: P.S. Shelton, School of Pharmacy, Campbell University, Dorothea Dix Hospital, 820 S. Boylan Ave., Raleigh, NC 27603, United States

SOURCE: Annals of Pharmacotherapy, (1997) Vol. 31, No. 5, pp. 533-542.

Refs: 43

ISSN: 1060-0280 CODEN: APHRER

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 020 Gerontology and Geriatrics

030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English; Spanish; French

ENTRY DATE: Entered STN: 970604

Last Updated on STN: 970604

AB OBJECTIVE: To test the reliability of drug utilization evaluation (DUE)

applied to medications commonly used by the ambulatory elderly. METHODS: A DUE model was developed for four domains: (1) justification for use, (2) critical process indicators, (3) complications, and (4) clinical outcomes. DUE criteria specific to use in the elderly were developed for angiotensin- converting enzyme (ACE) inhibitors and histamine2 (H2)-antagonists, and consensus was reached by an external expert panel. After pilot testing, two clinical pharmacists independently evaluated these medications, applying the DUE criteria and rating each item as appropriate or inappropriate. Interrater and intrarater reliability was assessed by using  $\kappa$  statistics. RESULTS: In a sample of 208 ambulatory elderly veterans, 42 (20.2%) were taking an ACE inhibitor and 56 (26.9%) an H2' antagonist. The interrater agreement for individual domains, represented by  $\kappa$  statistics, were 0.10-0.58 and 0-0.83 for ACE inhibitors and H2-antagonists, respectively. The  $\kappa$  statistic for overall agreement, which considered ratings from all criteria across all domains, was 0.24 for ACE inhibitors and 0.18 for H2-antagonists. Intrarater reliability was assessed 3 months later, and  $\kappa$  statistics were 0.61-0.65 (0.49 overall) and 0-0.96 (0.81 overall) for ACE inhibitors and H2- antagonists, respectively. CONCLUSIONS: Intrarater reliability for DUE was good to excellent. However, interrater reliability exhibited only marginal reproducibility, particularly where evaluators were required to use subjective judgment (i.e., complications, clinical outcomes). DUE may not be a suitable standard for assessing medication appropriateness in ambulatory elderly patients.

CT Medical Descriptors:

- \*drug utilization
- \*geriatrics
- \*prescription
- \*treatment outcome
- aged
- article
- congestive heart failure: DT, drug therapy
- drug indication
- duodenum ulcer: PC, prevention
- duodenum ulcer: DT, drug therapy
- esophagitis: DT, drug therapy
- gastroesophageal reflux: DT, drug therapy
- gastrointestinal symptom: SI, side effect
- human
- hypertension: DT, drug therapy
- hypotension: SI, side effect
- major clinical study
- oral drug administration
- priority journal
- reliability
- statistical analysis
- stomach ulcer: PC, prevention
- stomach ulcer: DT, drug therapy

Drug Descriptors:

- \*dipeptidyl carboxypeptidase inhibitor: AE, adverse drug reaction
- \*dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
- \*dipeptidyl carboxypeptidase inhibitor: PE, pharmacoeconomics
- \*histamine h2 receptor antagonist: PE, pharmacoeconomics
- \*histamine h2 receptor antagonist: DT, drug therapy
- \*histamine h2 receptor antagonist: AE, adverse drug reaction
- captopril: DT, drug therapy
- captopril: PE, pharmacoeconomics
- cimetidine: PE, pharmacoeconomics
- cimetidine: DT, drug therapy

enalapril: DT, drug therapy  
enalapril: PE, pharmacoeconomics  
lisinopril: DT, drug therapy  
lisinopril: PE, pharmacoeconomics

ranitidine: DT, drug therapy

ranitidine: PE, pharmacoeconomics

RN (captopril) 62571-86-2; (cimetidine) 51481-61-9,  
70059-30-2; (enalapril) 75847-73-3; (  
lisinopril) 76547-98-3, 83915-83-7; (ranitidine)  
66357-35-5, 66357-59-3

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ACCESSION NUMBER: 94151303 EMBASE

DOCUMENT NUMBER: 1994151303

TITLE: Understanding and treating Bartter syndrome.

AUTHOR: Gordon J.A.; Stokes III J.B.

CORPORATE SOURCE: Division of Nephrology, Department of Medicine, Univ. of  
Iowa College of Medicine, Iowa City, IA, United States

SOURCE: Hospital Practice, (1994) Vol. 29, No. 5, pp. 103-108+110.

ISSN: 8750-2836 CODEN: HOPRBW

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology  
005 General Pathology and Pathological Anatomy  
006 Internal Medicine  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 940608

Last Updated on STN: 940608

AB Most of its clinical manifestations are the result of hypokalemia. The  
diagnosis is one of exclusion, mainly of surreptitious vomiting and  
diuretic abuse. The primary cause remains unknown but the most likely  
candidate is reduced sodium chloride reabsorption in the thick ascending  
limb of Henle's loop Current therapy focuses on multiple agents to reduce  
massive potassium loss.

CT Medical Descriptors:

\*bartter syndrome: DT, drug therapy  
\*bartter syndrome: ET, etiology  
\*bartter syndrome: TH, therapy  
\*bartter syndrome: DI, diagnosis  
aldosterone blood level  
chloride transport

chronic diarrhea: DI, diagnosis  
clinical feature  
differential diagnosis  
diuresis

drug intoxication: DI, diagnosis  
henle loop  
human

hypokalemia: TH, therapy  
hypokalemia: ET, etiology  
hypokalemia: DT, drug therapy  
hypokalemia: DI, diagnosis  
magnesium deficiency: DI, diagnosis  
pathophysiology  
plasma renin activity  
potassium urine level

prostaglandin synthesis

renin angiotensin aldosterone system

review

sodium absorption

vomiting: DI, diagnosis

Drug Descriptors:

\*loop diuretic agent: PD, pharmacology

\*loop diuretic agent: DT, drug therapy

\*loop diuretic agent: CM, drug comparison

\*loop diuretic agent: CB, drug combination

\*potassium ion: EC, endogenous compound

\*potassium sparing diuretic agent: CM, drug comparison

\*potassium sparing diuretic agent: CB, drug combination

\*potassium sparing diuretic agent: DT, drug therapy

\*potassium sparing diuretic agent: PD, pharmacology

\*prostaglandin synthase inhibitor: PD, pharmacology

\*prostaglandin synthase inhibitor: CB, drug combination

\*prostaglandin synthase inhibitor: CM, drug comparison

\*prostaglandin synthase inhibitor: DT, drug therapy

\*sodium chloride: PK, pharmacokinetics

aldosterone: EC, endogenous compound

aldosterone: PD, pharmacology

amiloride: CB, drug combination

amiloride: PD, pharmacology

amiloride: DT, drug therapy

amiloride: CM, drug comparison

aminoglycoside antibiotic agent: TO, drug toxicity

angiotensin: PD, pharmacology

angiotensin: EC, endogenous compound

dipeptidyl carboxypeptidase inhibitor: CB, drug combination

dipeptidyl carboxypeptidase inhibitor: CM, drug comparison

dipeptidyl carboxypeptidase inhibitor: DT, drug therapy

dipeptidyl carboxypeptidase inhibitor: PD, pharmacology

ibuprofen: DT, drug therapy

ibuprofen: PD, pharmacology

ibuprofen: CM, drug comparison

ibuprofen: CB, drug combination

indometacin: PD, pharmacology

indometacin: CB, drug combination

indometacin: CM, drug comparison

indometacin: DT, drug therapy

potassium chloride: DT, drug therapy

potassium chloride: PD, pharmacology

potassium chloride: CM, drug comparison

potassium chloride: CB, drug combination

prostaglandin e2: EC, endogenous compound

prostaglandin e2: PD, pharmacology

prostaglandin synthase: EC, endogenous compound

renin: PD, pharmacology

renin: EC, endogenous compound

spironolactone: PD, pharmacology

spironolactone: DT, drug therapy

spironolactone: CM, drug comparison

spironolactone: CB, drug combination

triamterene: PD, pharmacology

triamterene: DT, drug therapy

triamterene: CM, drug comparison

triamterene: CB, drug combination

RN (potassium ion) 24203-36-9; (sodium chloride) 7647-14-5; (aldosterone)

52-39-1, 6251-69-0; (amiloride) 2016-88-8, 2609-46-3; (angiotensin)  
) 11128-99-7, 1407-47-2; (ibuprofen) 15687-27-1; (indometacin) 53-86-1,  
74252-25-8, 7681-54-1; (potassium chloride) 7447-40-7; (prostaglandin e2)  
363-24-6; (prostaglandin synthase) 39391-18-9, 59763-19-8, 9055-65-6;  
(renin) 61506-93-2, 9015-94-5; (spironolactone) 52-01-7; (triamterene)  
396-01-0

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ACCESSION NUMBER: 86211290 EMBASE

DOCUMENT NUMBER: 1986211290

TITLE: Gastrointestinal complications in critically ill patients: The intensivists' overview.

AUTHOR: Gottlieb J.E.; Menashe P.I.; Cruz E.

CORPORATE SOURCE: Yale University School of Medicine, Norwalk Hospital, Norwalk, CT, United States

SOURCE: American Journal of Gastroenterology, (1986) Vol. 81, No. 4, pp. 227-238.

CODEN: AJGAAR

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 038 Adverse Reactions Titles  
037 Drug Literature Index  
048 Gastroenterology  
006 Internal Medicine  
024 Anesthesiology  
009 Surgery

LANGUAGE: English

ENTRY DATE: Entered STN: 911210

Last Updated on STN: 911210

AB The critical care environment may be characterized by invasive monitoring, vasoactive drugs, and major interventions which may have adverse effects on gastrointestinal function. Furthermore, conditions such as heart failure or sepsis may compromise oxygen delivery to gastrointestinal organs. Life threatening illness from a variety of causes may produce endoscopically evident gastritis or ulceration in up to 100% of patients, and clinically evident bleeding in 20%. Clinical studies suggest that antacids or H2 receptor blockers may reduce the frequency of this complication. Other conditions are associated with a spectrum of hepatic dysfunction ranging from the cholestatic jaundice of reactive hepatopathy during sepsis to centrilobular necrosis and hepatitis of shock liver. Additionally, many drugs used in the critical care setting may adversely affect mesenteric oxygen delivery and result in ischemia or infarction of the bowel. An increased awareness and understanding of these and other gastrointestinal complications in critically ill patients will, it is hoped, lead to earlier detection and better therapy than is now available.

CT Medical Descriptors:

- \*adverse drug reaction
- \*cholecystitis
- \*confusion
- \*gastritis
- \*gastrointestinal symptom
- \*gastrointestinal toxicity
- \*gastroscopy
- \*intensive care
- \*intestine infarction
- \*intestine ischemia
- \*liver failure
- \*liver toxicity



\*neurotoxicity  
 \*shock  
 \*stomach acid secretion  
     **\*stomach ulcer**  
 \*stress ulcer  
 heart failure  
 jaundice  
 sepsis  
 survey  
 priority journal  
 digestive system  
 intoxication  
 psychological aspect  
 nervous system  
 stomach  
 cardiovascular system  
 liver  
 gallbladder  
 review  
 human  
 peripheral vascular system  
 large intestine  
 small intestine  
 diagnosis  
 heart  
 Drug Descriptors:  
 \*adrenalin  
 \*aminophylline  
     **\*angiotensin**  
 \*antacid agent  
 \*antihistaminic agent  
 \*arbaprostil  
 \*benzodiazepine derivative  
     **\*captopril**  
 \*carbenoxolone  
 \*cholinergic receptor blocking agent  
 \*cimetidine  
 \*digoxin  
 \*dopamine  
 \*growth hormone  
 \*histamine  
 \*histamine h2 receptor  
 \*histamine h2 receptor antagonist  
 \*isoprenaline  
 \*metaraminol  
 \*methoxamine  
 \*nitroprusside sodium  
 \*noradrenalin  
 \*oxygen  
 \*pentagastrin  
 \*phenylephrine  
 \*propranolol  
 \*prostaglandin e2  
 \*retinol  
 \*vasoactive agent  
 \*vasoconstrictor agent  
 (adrenalin) 51-43-4, 55-31-2, 6912-68-1; (aminophylline) 317-34-0; (  
**angiotensin**) 11128-99-7, 1407-47-2; (arbaprostil) 55028-70-1; (  
**captopril**) 62571-86-2; (carbenoxolone) 5697-56-3,

RN

7421-40-1; (cimetidine) 51481-61-9, 70059-30-2; (digoxin) 20830-75-5,  
57285-89-9; (dopamine) 51-61-6, 62-31-7; (growth hormone) 36992-73-1,  
37267-05-3, 66419-50-9, 9002-72-6; (histamine) 51-45-6, 56-92-8,  
93443-21-1; (isoprenaline) 299-95-6, 51-30-9, 6700-39-6, 7683-59-2;  
(metaraminol) 33402-03-8, 54-49-9; (methoxamine) 390-28-3, 61-16-5;  
(nitroprusside sodium) 14402-89-2, 15078-28-1; (noradrenalin) 1407-84-7,  
51-41-2; (oxygen) 7782-44-7; (pentagastrin) 5534-95-2; (phenylephrine)  
532-38-7, 59-42-7, 61-76-7; (propranolol) 13013-17-7, 318-98-9, 3506-09-0,  
4199-09-1, 525-66-6; (prostaglandin e2) 363-24-6; (retinol) 68-26-8,  
82445-97-4